THE MEDICAL JOURNAL OF AUSTRALIA

VOL. I.—35TH YEAR. SYDNEY, SATURDAY, JANUARY 10, 1948. No. 2.

Table of Contents.

[The Whole of the Literary Matter in THE MEDICAL JOURNAL OF AUSTRALIA is Copyright.]

ORIGINAL ARTICLES— Page.
The Edward Stirling Lectures—I. The Basis of Allergic Disease, by F. M. Burnet 29
After-Care in Radical Amputation of the Breast, by W. Maxwell 35
Artificial Pneumothorax and Internal Pneumolysis, by Alan King 38
Struma Ovarii Accompanied by Thyreotoxicosis, by K. A. McGarrity and L. F. Dodson 42

REVIEWS—
Clinical Laboratory Methods 44
The Physiology of Woman 44

LEADING ARTICLES—
The Federal Council: A Plea for Action 45

CURRENT COMMENT—
Collapse following Exertion 46
Revolt from the Bedpan 46
War Wounds of the Head 47

ABSTRACTS FROM MEDICAL LITERATURE—
Gynæcology 48
Obstetrics 49

BIBLIOGRAPHY OF SCIENTIFIC AND INDUSTRIAL REPORTS—
The Results of War-Time Research 50

BRITISH MEDICAL ASSOCIATION NEWS—
Scientific 52

POST-GRADUATE WORK— Page.
The Post-Graduate Committee in Medicine in the University of Sydney 54

NAVAL, MILITARY AND AIR FORCE—
Appointments 54

CORRESPONDENCE—
New Treatment of Rheumatoid Arthritis 54
Nurses: Their Recruitment and Training 54
Zeitschrift für Vitaminforschung 55
The Role of Spinal Fusion in Arthrogenic Sciatica 55
A Social Aspect of the Rh Factor 55
Poliomyelitis in Preventive Orthopædics 55
Concerning the Pathology and Treatment of Tennis Elbow 55

OBITUARY—
Herbert Huff Johnston 56
Alfred Jefferis Turner 56
William John Stewart McKay 56
David Neilson Knox 56

NOMINATIONS AND ELECTIONS 56

BOOKS RECEIVED 56

MEDICAL APPOINTMENTS 56

DIARY FOR THE MONTH 56

MEDICAL APPOINTMENTS: IMPORTANT NOTICE .. 56

EDITORIAL NOTICES 56

The Edward Stirling Lectures.

I. THE BASIS OF ALLERGIC DISEASE.[1]

By F. M. BURNET,

Director of the Walter and Eliza Hall Institute of Research in Pathology and Medicine, Melbourne.

ALLERGIC DISEASE is a rather vague and elastic term which may mean different things to different people. I should define it for the purposes of this lecture as a term covering those conditions which are associated with the inappropriate activity of immunological processes in the human body. The range of conditions includes with certainty acute anaphylactic reaction (sometimes fatal), serum sickness, sensitization to a wide variety of common environmental proteins, polysaccharides *et cetera* (manifested by variants of the hay fever, asthma, urticaria types of reaction) as well as sensitization to simpler chemicals (for example, formalin and aspirin) which can unite with body protein to form an antigenic complex. In all these conditions we have a production of symptoms and associated lesions by the contact of certain body tissues with a rather wide variety of substances.

Then there is a less clearly defined group of conditions in which allergy is provoked by a microorganism and the clinical picture is essentially a complex of allergic and infective processes. *Erythema nodosum* is a typical allergic manifestation of this group; but more widely we can say that the two common basic causes of *erythema nodosum*, tuberculosis and subacute streptococcal infection, are practically always associated with some allergic manifestations—so much so that reinfection tuberculosis and rheumatic fever cannot be approached from any other angle than as combined allergic-infective diseases. The majority of cases of asthma occurring in the second half of life can also be included in this group, and though my knowledge of dermatology is of the slightest, I gather that combined infective-allergic processes are probably concerned in most of the subacute and chronic skin diseases.

Finally there is a much more dubious group of degenerative diseases, in which there are strong suggestions that the body is producing antibody against some of its own constituents. None of these interpretations are established; but I feel reasonably certain that a large proportion of nephritic conditions and a number of demyelinating diseases of the central nervous system have in part at least a basis in some inappropriate immunological activity.

My object in this lecture is to provide the theoretical basis that is needed for a partial understanding of these varied disease conditions. It is not likely that I shall succeed—my approach is only that of a theoretical immunologist with a considerable range of interest and experience in the problems of infection and immunity at the laboratory level. As such I shall undoubtedly be tempted to provide generalizations that will unduly simplify the position. If this happens, my excuse must be that it is better to have clear ideas, which may need serious revision in a year or two, than to try to retain an uncoordinated mass of detail without such clarification.

The point of view which I shall adopt can be briefly outlined as follows.

As part of the necessary mechanism of defence against invasion by microorganisms, vertebrates, including ourselves, have developed the capacity to respond to a temporary failure of such defences by the development of substances—antibodies—specifically adapted to deal with the infecting agent in question. The specificity of the response depends on the chemical pattern of certain components of the microorganisms concerned. Such immunological responses necessitate a delicate capacity

[1] Delivered on August 26 and 28, 1947, at Adelaide.

to differentiate between foreign organic material and the proteins and other complex substances proper to the body, particularly as the cells concerned in the immune process have other functions, notably in removing effete and damaged body cells, in combating infection non-specifically and in the processes of repair. These are nearly all emergency rather than routine functions, and in view of the great variety of traumatic and infective emergencies to which the body is exposed, it is amazing how effective in general the bodily response can be. But the immunological mechanism is a mechanism and it is not infallible. It may "mistake", for example, the chemical pattern of a pollen grain or of an industrial chemical for the pattern of a pathogenic bacterium, and the corresponding response, which might be appropriate in preventing reinfection with a bacterium, may be most inappropriate to renewed contact with the real stimulus. My thesis will be that by and large the allergic diseases are manifestations of such "mistakes" by a mechanism which under the best conditions needs to be very finely adjusted to function effectively against the common emergencies. The commonest basis for its "mistaken" activity is genetic; minor and otherwise insignificant variations in chemical details of cellular enzymes may make some foreign "molecular pattern" quite inappropriately effective as a stimulus to a useless and embarrassing immunological response.

I shall start with a discussion of the nature of antibody production and of the different types of antibody, and I shall be particularly concerned with the way modern genetic theory is indicating how antibody production could be modified as a result of genetic differences. The second section will be concerned with sensitization phenomena, the actual pathological basis of allergic symptoms, and the third with the experimental and theoretical basis for current methods of treatment.

The Production of Antibody.

It is one of the basic properties of living matter to be able to differentiate between what is its own substance and what is not. An amœba engulfs and digests a foreign microorganism with ferments which do not damage its own, essentially similar, substance. When two primitive types of sponge, recognizably different by virtue of different pigments, are disintegrated into single cells and the cells mixed in a dish of seawater, red cells adhere to red cells and yellow to yellow, forming little buds of tissue from which the appropriate sponge can be redeveloped. Recognition of "self" from "not self" in this sense is probably the basis of immunology. I have suggested that it is linked up with the most basic of all living processes, the synthesis, or I would prefer the replication, of essential enzyme-protein within the cell.

However that may be, the fact remains that throughout the animal kingdom organisms (*a*) utilize the tissues of other organisms for food, often employing intracellular digestion methods, and (*b*) are exposed to parasitic invasion which they resist essentially by digesting the invader. Both activities obviously require the basic ability of cells to differentiate between self and not self, and equally obviously this differentiation must be based on finely adjusted enzyme specificities, especially of proteinases—that is, the enzymes which break down and perhaps synthesize proteins within the cell.

At the present time there is an important revolution going on in biochemistry which has not yet reached the textbooks and which has created hardly a ripple in clinical teaching or practice. This is the development of biochemical genetics. Until very recently biochemistry was virtually concerned only with what goes into the living machine and what comes out—it had no approach to the real chemistry of the cell by which its structure is compounded and by which it guides all the less important reactions with which biochemistry has been concerned. About five years ago G. W. Beadle, of Stanford, found a way by which this real biochemistry of the cell could be approached. What was needed was a simple microorganism with well-defined chemical growth requirements and a straightforward type of bisexual reproduction. The mould neurospora, one of the types found on mouldy bread, supplied these needs admirably. Then by a technique of isolating and hybridizing variants with differing chemical requirements, which I need not describe in detail, Beadle and his collaborators found themselves in possession of a method of correlating genetic changes with chemical reactions within the cell. I do not want to mention anything at all about the actual processes with which they were concerned, but I must stress the extremely important generalization that Beadle has propounded: that each gene is concerned with a single type of enzyme action. Perhaps one of the most impressive examples of this comes not from neurospora but from man. There is a type of congenital idiocy which is associated with and apparently due to the absence of an enzyme (phenylpyruvic oxidase) concerned in the breakdown of tyrosine. The genetic behaviour of the disease indicates that affected individuals differ from the normal by a single gene. The active form of the gene concerned is missing from every cell of the body and equally the enzyme; the accumulation of phenylpyruvate within the cells of (part of) the central nervous system is presumably responsible for the mental deficiency characteristic of the condition.

I seem to be getting far away from allergy and antibodies, but I am not; allergy is a matter not only of antibodies but, as you all know, of heredity also. Somewhere in this work of Beadle's and his followers will eventually be found a more precise answer to the

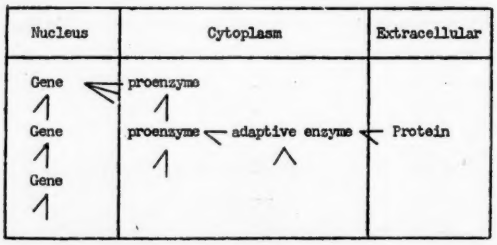

FIGURE I.

A highly schematic interpretation of Beadle's hypothesis of gene-enzyme relationship as applied to the nature of antibody production. Replication is indicated vertically, "partial replication" horizontally.

problems of allergy than the crude outline I am trying to formulate. The next step in the argument is more speculative. It is that the cell enzymes are as it were direct descendants of the corresponding genes that control their activity. It is believed that in addition to producing with every cell division two complete replicas of itself, a gene also produces partial replicas by a similar process. The nature of the process of gene, enzyme or virus replication is the "top secret" of biochemistry; but there is no doubt about its occurrence. The partial replicas have in their turn limited powers of self-replication. (Replication is equivalent to multiplication or reproduction, but the word has a neutral character lacking in the other two.) At one, two or more removes from the gene they represent the working enzymes of the cell.

For the next step in the argument, we have to turn to adaptive enzymes. You are all aware that the Gram-negative intestinal bacteria are classified very largely by their "sugar reactions"—that is, by their possession of enzymes capable of fermenting some of the sugars used in the conventional series of tests. If the tests are made with "resting" bacteria—that is, with washed living organisms suspended in a dilute solution of the sugar being tested—two types of reaction may be noted. A coliform bacillus has been grown in glucose broth and then washed and tested against glucose, fructose, mannose, sucrose and lactose. It starts fermenting the first three immediately and the other two only after an hour or

two's delay. If, however, the same strain is grown in lactose broth, washed and tested, lactose also is fermented immediately. The bacillus then is said to contain constitutive enzymes capable of splitting glucose, fructose and mannose and to be capable of producing adaptive enzymes against sucrose and lactose.

Very recently Lindegren and Spiegelman have shown that an adaptive enzyme in yeast can multiply in the cytoplasm irrespective of the presence or absence of the nuclear gene which determines its initiation, provided that its particular substrate remains in the environment.

We reach then a picture of the living cell as a nest of ferments in Sherrington's phrase. It is probably true that apart from some structural and reserve material, all the protein in a living actively metabolizing cell like a leucocyte or a liver cell is enzymically active, and that much of it still retains the power of self-replication when required. Further, many of the enzyme mechanisms may have a certain adaptability—a proteinase normally dealing with a certain protein may find itself in contact with a related but not identical protein, and by a process equivalent to the appearance of adaptive enzymes change its character to "fit" the new substrate more effectively.

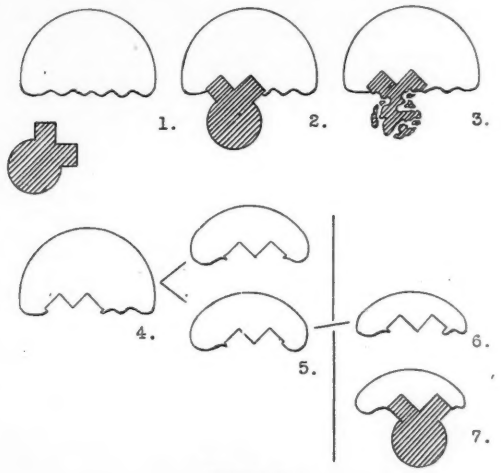

FIGURE II.

Diagrammatic representation of an hypothesis of antibody production involving the formation and replication of adaptive enzymes. Specificity is represented by the complementary patterns on antigen (shaded) and enzyme (1 to 4) or antibody (6 and 7).

I think you will now see how the argument has come back to the problem of self and not self with which I started. When an alien protein molecule finds itself within a living cell, it is in the midst of a coordinated series of enzymes, largely proteinases, whose mutual destructiveness is curbed by some system of specific checks that we cannot particularize, but some of which with or without preliminary adaptation can destroy the alien molecule.

One way of looking at the production of antibodies as a result of the entry of foreign material into the body is to regard it as a manifestation of this process of intracellular digestion of alien protein (or polysaccharide or perhaps lipid). On this view the antibody liberated into the blood-stream is a final stage in the series of partial replicas produced by a certain gene or series of genes. The penultimate stage is the enzyme or complex of enzymes that produces γ globulin molecules. This is highly adaptive in character, and once the enzyme complex has dealt with an unusual substrate, a specific modification complementary to the molecular pattern of that substrate is induced in the complex. Antibody is the product of replication and liberation of these modified enzymes.

That, expressed very briefly and necessarily rather crudely, is my own picture of how antibody is produced. It is not the orthodox view. The orthodox view is that antibody is serum γ globulin that has been synthesized in the cell in spatial contact with the antigen or significant portions thereof. As a result the ends of the molecule have a complementary pattern (lock-key, die-coin relationship) which will result in their specific union with antigen subsequently met. For a discussion of the pros and cons of the two theories you will have to go to textbooks of immunology.

The Different Types of Antibody.

Immunology is a very complex and rather difficult subject, and its intricacies are by no means exhausted by an enumeration of all the different types of antibody that can be produced by appropriate immunization of man or rabbit and recognized by the orthodox test-tube techniques. Such classical antibodies are the bacterial agglutinins, the precipitins and complement-fixing antibodies and the virus-neutralizing antibodies. These antibodies are well characterized γ globulins which function in the test-tube as bridges between antigen molecules or particles. They are recognized either by the primary aggregation produced or by secondary results of the aggregation such as complement fixation.

In man and rabbit they are globulins of about 160,000 millimicrons. They are predominantly produced by

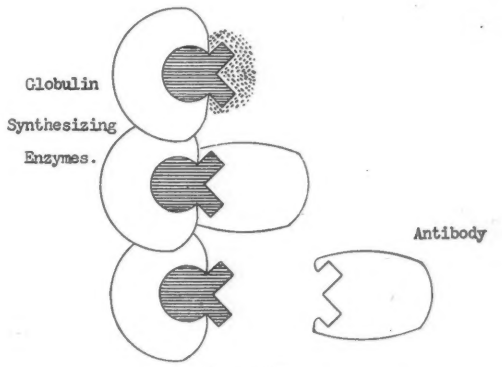

FIGURE III.

A similar diagram of the Haurowitz, Mudd-Pauling hypothesis of antibody production. Note that in Pauling's version the specific pattern is impressed on both ends of the antibody molecule instead of only one as shown here.

lymphoid tissue, lymph nodes and spleen. They are taken up by the tissues to a moderate extent, but pass readily through the placenta and are found in the cord blood to about the same titre as in the mother's blood.

Also present in the blood are, or may be, two other types of antibody. The first is antibody of the antitoxin type such as diphtheria or tetanus antitoxins. It is not certain whether this is quite distinct from the first class, but there are physical differences and what evidence there is suggests that the antibody is not produced in lymphoid tissue. The second type includes the A B O blood group agglutinins and the Wa antibody. Apart from the fact of their physical differences including much higher molecular weight, nothing is known about their significance. They are detected in similar fashion to the classical Type I antibodies, but they do not pass the placenta, or pass it only in a very small amount. These three types of antibody might be called Types I*a*, I*b* and I*c*.

The next type to be considered is the type of most direct interest to allergists. This is the antibody associated with sensitization to pollen, food substances and so on. Such antibody is not detectable by the ordinary type of test-tube reactions. Its presence in the serum can be detected only by the Prausnitz-Kustner method of passive

transfer to human skin. The major characteristic of this Type II antibody is its fixation in tissues on which it confers characteristic reactivity with the antigen. It fails to pass the placenta. The site of its production is not known with certainty. It is not the lymphoid tissues concerned with Type I antibodies, since pollen extracts given parenterally produce Type I protective antibody, not the Type II sensitizing antibody. My guess would be that these antibodies are produced by the monocytic mesodermal cells found in the subepithelial layer of mucous membranes. The methods for their detection and quantitative measurement are so tedious (passive sensitization in human subjects) that no studies have been made of their physical character. A method for in-vitro estimation of this type of antibody would for very many reasons be of the greatest value.

A third major type of antibody is characteristic of certain subacute infections associated with extensive monocytic accumulations around the lesions and in infected lymph nodes. The evidence that the antibody exists at all in the circulating blood is restricted to the results of a few experiments in animals; but indirectly it seems certain that the antibody does in fact circulate, but is so rapidly fixed to cells that only a very low concentration can ever exist in the blood. Type III antibody is characteristically produced in tuberculosis, subacute streptococcal infections, brucellosis, coccidioidomycosis and *lymphogranuloma inguinale*. *Erythema nodosum* is characteristic of the early phase of sensitization, and the characteristic skin reaction is of the long-lasting tuberculin type. The evidence is almost conclusive that the sensitizing agent or antibody is produced in the inflammatory mesodermal cells surrounding the source of antigen.

It is unlikely that there are other major types of antibody; but even with three it is obvious that there are many opportunities for complication and for difficulties of interpretation. Neither a pollen grain nor a bacterium is a simple substance. More than one form of Type I antibody may be produced, and particularly in the case of infection, opportunities may be afforded for more than one type of antibody to be produced. It is general to find that after an acute infection—for example, mumps or typhoid fever—in addition to circulating antibodies of appropriate character, a low-grade skin reactivity has appeared. It is usually an erythematous reaction without the acute weal and flare of a typical allergic reaction and much less prolonged and intense than a positive tuberculin reaction. It is not known whether these reactions merely represent a weak sensitization of tuberculin type, or whether an intermediate type of antibody is involved.

As far as clinical work is concerned, it is probably adequate to consider only the three major types of antibody and their accompanying skin sensitization.

Tissue Reactivity and the Clinical Manifestations of Allergy.

It is not easy to offer a clear statement about the tissue hypersusceptibility that is or may be associated with the development of each kind of antibody. A beautifully worked out explanation of anaphylaxis in guinea-pigs is available in all the textbooks, but this explanation is only very partially applicable to conditions in man. Serum sickness is the nearest equivalent. This is a familiar enough condition, and particularly after an intravenous injection it may be very severe. The essential features are a six to ten day incubation period, lymph gland enlargement, an urticarial or erythematous rash, joint pains and fever. The interpretation of these symptoms is that they result from the interaction in the tissues of antigen (horse serum molecules) and actively produced human antibody—that is, horse serum precipitins. When a small dose of foreign serum has been given locally (for example, intradermally in the forearm), serum sickness may be purely local and may take the form of an itchy urticarial swelling over and around the inoculated area. It seems therefore that in general the antigen (the foreign protein) is present in the tissues, and that when antibody comes into circulation, it penetrates at certain points through the endothelium to react with the antigen. Actually there is a good deal of obscurity about the details of reaction when both antigen and antibody are present in the body. All that can be safely said is that when antigen and antibody of Types I and II react in sufficient concentration in or on tissue cells, cell damage is induced which is normally associated with liberation of histamine. In the skin intradermal injection of histamine, or acute liberation of histamine as a result of some other process, gives the characteristic triple response of Lewis—erythema, weal and flare.

The standard skin test procedures of the allergist are most readily and probably correctly interpreted as a method of bringing the antigen into contact with cells which have taken up antibody from the blood. If specific union occurs, histamine is liberated and diffused through the local tissues, producing the triple response. It is probable that this response is given by any Type I or Type II antibody which is present in sufficient concentration in the skin, provided that the corresponding antigen is available in soluble form. Type II antibodies are especially effective because they are automatically as it were taken up from the blood into the tissues, while Type I antibodies are characteristically retained in the body fluids.

The clinical manifestations of the common allergic diseases are essentially similar in their pathogenesis to the diagnostic skin tests, but it seems that to account for them adequately we must assume that in addition to histamine other pharmacologically active substances may be liberated in or from the cells where the antigen antibody reaction occurs. Pollen antigen reacting with nasal mucosa sensitized by antibody gives rise to congestion œdema and hypersecretion of serous fluid. Poison ivy antigen coming into contact with the skin of a sensitized individual provokes urticarial dermatitis. An egg-sensitive child comes out in urticarial blotches at those points where antigen in the blood by one circumstance or another comes into effective contact with antibody in the tissues. To judge by the response obtained to the antihistamine drugs that I shall mention later, urticarial manifestations of allergy are almost wholly due to histamine liberation. By the same criterion hay fever is by no means entirely a result of histamine liberation, and asthma is probably due to a different and at present unknown mechanism. Spasm of bronchial and bronchiolar musculature is undoubtedly one component of asthma, and in the guinea-pig acute anaphylactic types constriction of this musculature is a characteristic response to histamine. But in man the process seems to be considerably more complex. Mucus secretion with associated obstruction of the bronchiolar airways seems to be of special importance, and in persons dying of or with asthma the histological picture is usually one of increased mucus secretion, infiltration with eosinophile leucocytes and hypertrophy of bronchial musculature.

The part played by the eosinophile leucocyte is a challenge to pathology. As far as I know the immunological significance of the eosinophile cell has never been elucidated. It is undoubtedly associated in some way with hypersensitivity. With the development of a weal reaction from say pollen on the skin, the majority of the leucocytes passing into the tissue spaces are said to be eosinophile. Allergic processes in the lungs including asthma are associated with a raised eosinophilic cell count in the blood; helminthic infections probably provoke eosinophilia essentially because of the sensitization phenomena that are commonly associated. Since there appears to be no place for the eosinophile leucocyte in the theory of hypersensitivity that I have been discussing, it seems that this theory must be seriously incomplete if not wholly wrong. For a young pathologist who wants a first-rate problem, I would suggest this theme of the nature of the eosinophile leucocyte. What I cannot tell him is how he might approach the experimental side of the problem.

The type of hypersensitivity associated with the rather hypothetical antibody of Type III that is responsible for tuberculin and similar hypersensitivity, is the only one in which very clear evidence of the presence of antibody in the cell and of the directly damaging effect of contact with antigen can be given. If tissue cultures are prepared of mesenchymal cells from the spleen of normal and of tuberculous guinea-pigs respectively, these can be differentiated at once by observation of the effect of a weak concentration of tuberculin on the cells migrating from the tissue fragment. The cells from the tuberculous pig are damaged or killed, those from the normal animal are unaffected. The nature of the process induced is unknown. Presumably some pharmacologically active substance is activated or released by antigen-antibody union and immediately or indirectly gives rise to the syndrome that appears as a positive tuberculin reaction.

The Genetic Aspects of Allergy.

The essence of allergic disease is its individuality. Extensive enough inquiry will show that some time or other most adults have experienced some allergic symptoms, but those who are severely affected are few, and amongst these few an extraordinarily wide range of antigens is responsible. What are the factors which determine that one in a thousand individuals is sensitive to strawberries, one in twenty to ryegrass pollen—that a proportion only of chemical workers will become sensitized to some organic solvent to which they are all exposed, and so on?

The answer can be given only in a very general fashion. In the first place, there is reasonable agreement that all hypersusceptibilities that are clinically or experimentally demonstrable are acquired by effective previous contact with the allergen or with some substance having immunologically equivalent structure.

Some allergens seem to be of higher intrinsic sensitizing capacity than others, the circumstances of industry may give concentrated and prolonged opportunity of sensitization, and these and similar circumstances will be reflected in the proportion of persons with frank allergic symptoms. But the individual predisposition will always be evident, and it seems probable that 90% of individual differences in this respect are due to genetic factors.

I suppose that somewhere or another there are reports on twin studies in allergy, but I have been unable to find them. If they are non-existent, this lack should provide a valuable opportunity to a group of allergists. For an outstanding problem is to determine whether an allergic inheritance provides merely a general predilection towards sensitization, as is generally thought, or a more limited susceptibility to sensitization by one particular group of chemical entities. Since identical twins are genetically similar in all respects, it would be most illuminating to examine the identical co-twins of a dozen patients with some allergic manifestation. My own feeling is that there would be a closer similarity in the type of sensitization than would be expected on current ideas. I may be wrong. The evidence I have in mind is the well-known irregularity with which individual rabbits or human beings respond to the same immunizing procedure. I remember discussing this point with Heidelberger in New York. He was using pure pneumococcal polysaccharides corresponding to the commonest infecting types in man as possible immunizing agents against pneumonia. As part of the investigation, the antibody responses of volunteers and of rabbits to the mixed vaccine of five polysaccharides were studied. Some individuals gave a good response to three or four of the antigens, others to only one, but with no regularity as to which one. The only regularity in the business that Heidelberger could see was that, though both human beings and rabbits gave completely irregular responses, the two species were irregular in the same sort of way.

It may be worth while to speculate a little as to how genetic differences can be reflected in variations in reactivity to casually encountered foreign substances. To do so will require a little preliminary consideration of how genetic differences in general arise.

Mutations are constantly occurring in human as in any other types of genetic mechanism, and the more refined the method of study, the more frequently will mutations be detected. Most mutations are deleterious and are normally recessive, so that they remain underground until chance brings two recessive genes together with lethal or other unfortunate manifestations in the offspring. Seriously damaged genes will eventually be eliminated by the failure to survive or to reproduce of those homozygous for the recessive gene. But there are infinite possibilities of non-lethal neutral or nearly neutral mutations. One has only to consider again the time-honoured examples of the breeds of dogs or the variety of human countenance and temperament to realize this.

It is probable that in the fine genetic chemistry of the body there is a certain elasticity, a small margin of error, within which changes can be tolerated or appropriately adjusted for. In an intracellular enzyme molecule, it may be essentially immaterial whether one or two amino-acid residues are interchanged or absent. The general mechanism of the body will go on working normally; but nevertheless I believe that it is because of minor chemical changes in enzyme character that we have the allergic inheritance.

We must remember how delicately balanced this business of the recognition of self and not self is within the body. In addition to dealing with frank parasitic invasion, the body has to deal with what is probably a fairly constant ingress of sub-pathogenic organisms and partially digested protein molecules from the bowel, and in addition has to finalize the account of a vast number of its own expendable cells by the same essential process. There is a great deal of current controversy as to whether hypersensitivity is ever of any "use" to its possessor. Rich, for instance, has argued very cogently for the essential harmfulness of allergy from the point of view of the person infected with tuberculosis, and I do not think that there has been any satisfactory counter to his arguments. But in considering the evolution of a physiological character of the animal body, it is always necessary to think of the natural, frequently recurring, situations in which the presence of the character would be of sufficient survival value to be developed by natural selection. I have suggested previously that hypersensitivity may have been basically evolved as a means of rendering defence processes more rapid and efficient in dealing with the everyday emergency of traumatic damage and potential infection by low-grade pyogenic organisms present on the skin or mucous surfaces. A mechanism very effective for dealing with a local emergency may be the worst possible one for the body when called into general action as in anaphylaxis or septicæmic infection by a stimulus applied over the whole body. One might use the simile of a set of warehouses equipped with automatic fire sprinklers delicately adjusted to come into action at any rise of temperature above the normal. This may be able to deal very effectively with a local fire and produce only a minor amount of incidental damage. But if a local fire got out of control and hot air swept through the whole of the warehouses, setting all the sprinklers into action simultaneously, the mechanism would function in a way positively harmful to the purpose for which it was designed. And if we want to, we can extend the simile to provide a picture of what happens when the body is invaded by an organism which readily provokes allergic reactivity and by subsequent reaction with sensitized cells does most of its actual harm—the tubercle bacillus, for example; merely change the contents of the warehouses from timber or textiles or tea to calcium carbide or strong sulphuric acid and you can realize how a mechanism designed for one purpose and serving it well may be positively dangerous when it is called into action by an inappropriate stimulus.

This digression is merely to stress the fact that the immunological mechanism of the body must necessarily be a delicately balanced compromise affair, even when in its most effective genetically normal form as moulded by evolution and natural selection. Any minor change in the genetic mechanism which is reflected in the structure of an enzyme involved in the immunological process may have an incommensurately great clinical effect. I fancy that the man sensitive to strawberries is simply someone with an intracellular enzyme which, by mere genetic accident, is different from the normal in such a way that it has a special facility for reacting with some molecular configuration in the strawberry protein concerned. It will probably be a long time before such a conception of the genetic basis of allergy can be rigorously demonstrated; but I have little doubt that some general conception of this sort will eventually be accepted.

This general idea of the delicate balance of the immunological mechanism leads at once to another growing point in medicine—the possibility that some of the degenerative-inflammatory processes without known ætiological agents may also be inappropriate manifestations of immunological activity.

This is an idea which has been current in speculative form for a good many years, but has had very little experimental backing until recently. A great deal of interest has been aroused by the possibility of inducing acute degenerative and demyelinating changes in monkeys by "immunizing" them with central nervous system substance—even with monkey central nervous system substance. In fact, one of the recent investigations arose out of an attempt to immunize monkeys against poliomyelitis. Many previous trials of immunization have been made, most of them with either a negative result, or producing only a very limited degree of immunity. The problem was reopened because of the recognition that by the use of certain adjuvants inoculated with an antigen a more prolonged immunity or antibody response resulted. I think this idea was first exploited by Ramon for increasing the yield of antitoxin in horses; he used for the purpose tapioca—why, I cannot imagine. Freund, who popularized the idea in America, mixed his antigen with paraffin oil and killed tubercle bacilli, using a lanoline base to emulsify the components to a cream. When such an antigenic mixture is injected it acts as a mild irritant, causing a marked cellular reaction predominantly of fibroblasts and macrophages. Absorption of the antigen is slowed, and probably largely on account of the prolonged antigenic stimulus a much greater and longer lasting production of antibody results. However, when monkey brain substance (containing poliomyelitis virus—but that was immaterial) was emulsified with Freund's adjuvant mixture and inoculated in monkeys, the animals became ill within a few weeks, and on examination showed gross hæmorrhagic and demyelinating lesions in the central nervous system.

Pathologically similar lesions are seen in human subjects of acute disseminated encephalomyelitis, and as far as my reading goes there is no clear line of demarcation between this condition and the various grades of disseminated sclerosis. The resemblance may be accidental; but after all some interpetation of disseminated sclerosis must eventually be adopted, and this experimental work offers a basis for such an interpretation. It is simply that in certain individuals the normal scavenging process, by which damaged cells are eliminated, is switched into an inappropriately immunological process—an auto-antibody directed against some specific component of, say, damaged nerve cells is produced. This causes damage presumably by interference with intracellular enzyme mechanisms when it reaches cells of appropriate type in the central nervous system. It may be that in this way further antigen is liberated, so that a vicious circle is developed. In the absence of direct observational evidence, the speculative details can be filled in to taste. But what I would stress is that this particular distortion of immunological function is very rare, and almost certainly depends (i) on an innate genetically determined abnormality, and (ii) on some probably minor damage in the central nervous system, giving rise to the initiating antigenic stimulus. This is all speculation; but I would contend that if in the normal animal we can produce this highly "unadaptive" response to brain tissue by intensifying its antigenic effect with adjuvants, then it is equally possible that an appropriate genetic interference with the immunological mechanism in man might allow "auto-sensitization" to brain tissue to become manifest in a small proportion of persons.

The Basis of Treatment of Allergic Disease.

The obvious first line of approach to the alleviation of allergic symptoms is to find the responsible allergen and avoid the occasion of contact with it. This is a matter of persistence, detective work, ingenuity and common sense, which has nothing to do with the physiological background. When, as is very often the case, avoidance is impossible, treatment is reducible to three essential types: (i) pharmacological relief of symptoms, especially by adrenaline and related drugs; (ii) the use of the recently developed antihistamine drugs; (iii) immunological treatment (desensitization).

1. I have nothing to say in regard to the use of adrenaline, ephedrine and such local vasoconstrictors as benzedrine. Their action is based on the normal pharmacological principle of counteracting the symptom-producing process by an opposing effect on the tissue concerned.

2. The newly developed antihistamine drugs are of greater theoretical interest. It has been shown that a number of organic compounds with a certain, though to an outsider rather remote, structural resemblance to histamine, have a well-marked antihistamine effect in laboratory animals. The three forms that are commercially available all have a dimethyl-ethylamine end group attached to a complex that varies from one drug to the other. Their effectiveness in preventing fatal histamine spasm in the guinea-pig increases in the following order: "Benadryl", "Pyribenzamine", "Neoantergan" or "Anthisan". The guinea-pig is so sensitive to histamine, to which it responds primarily by an intense usually fatal bronchospasm, that it provides a very useful means of assaying such drugs. There is no question at all that they have a potent antihistamine effect, and since they are very effective in the guinea-pig when given as aerosols by inhalation, they appear to act by rendering the smooth muscle cells non-reactive to histamine reaching them through the blood-stream. In human clinical practice the drugs have proved themselves of great value in the treatment of acute allergic urticaria, and subject to the necessity for continuous use, in many cases of chronic urticaria. They have been less successful in hay fever and are virtually useless in asthma.

This failure to control the allergic manifestations in the mucous membranes of the upper and lower parts of the respiratory tract is one of the lines of evidence which suggests that something more than histamine release is concerned in the pathology of asthma.

Antihistamine drugs do not act like adrenaline *et cetera* by producing pharmacological responses diametrically opposed to those induced by histamine. In the normal animal they may produce no effect at all, and probably act by blocking the access of histamine to some effector mechanism of the reactive cells. In general they are effective only so long as the drug is present in sufficient concentration in the circulating blood. They are purely symptomatic remedies, whose main usefulness is in dealing with acute episodes, particularly of urticarial type.

The chief undesirable side-effect which has been described is drowsiness, which may sometimes be so severe as to render the use of the drugs undesirable.

3. The rationale of desensitization is difficult to decipher, and in all probability a number of processes are concerned in a satisfactory therapeutic result. The most important mechanism is probably that described by Cooke, Loveless

and others. They showed that in ragweed-sensitive patients desensitization by parenteral injection of specific extracts was not comparable to desensitization as carried out in the anaphylactic guinea-pig. What was being done was the stimulation of a second type of antibody—a Type I antibody according to the scheme I suggested earlier. It is an antibody which does not readily become fixed to cells, and when it reacts with a molecule of the specific allergen, this is rendered incapable of subsequent reaction with fixed Type II antibody. This work provides a rational basis for attempts at desensitization, but it is unlikely to be the whole story.

The general reactivity of the tissues can be modified by many agents. A typical example is the temporary abolition of skin reactivity after an attack of measles—this will render even a positive reactor to tuberculin temporarily "negative". A number of mildly toxic agents might therefore be capable of non-specifically reducing reactivity under favourable conditions. Here, or hereabouts, we come into debatable ground common to a great variety of the less well defined of human ills. When one reads of the number of sometimes successful treatments for such conditions as asthma, arthritis, migraine and eczema, the sceptic must feel that present-day physiological pathology does not help much in the field. Psychosomatic medicine is outside my field; but I feel very certain, partly from my own personal experiences as an allergic subject, that the occurrence of symptoms, their intensity and the degree of disablement they produce are all influenced by some factors in addition to the existence of the allergen and the hypersensitive cells. These factors, whether they are psychological or of some other origin, are as I have said outside my field, but I do not consider them any less important for that. In fact, I think it is likely that the doctor who can consciously or subconsciously recognize and remedy these factors may, at times, be of more benefit to his patient than the too scientifically-minded allergist.

Conclusion.

It must have been evident that I have talked not about allergic disease so much as about those aspects of the subjects I am interested in that have some bearing on allergy. My excuse is that only by so doing could I hope to say anything that is not immediately available in any textbook of the subject. Of all that I have said, the one thing that I should like to be remembered is my conviction that genetics and immunology are two sciences that in the immediate future are likely to be linked in a productive attack on some of the most fundamental problems of biology, and that out of such an attack may come knowledge of high significance for human medicine, not least in the field of allergic disease.

AFTER-CARE IN RADICAL AMPUTATION OF THE BREAST.

By W. MAXWELL,
Sydney.

Factors in Healing.

THE immediate desideratum following radical operation for mammary cancer is rapid healing of the whole traumatized area with an absolute minimum of scar tissue formation. This area is made up of the deep raw surfaces of the skin flaps applied to the bared chest wall and the lateral and posterior walls of the cleared-out axilla.

Among other things, rapid healing may be expected to render post-operative irradiation the more effective as this latter depends perhaps as much upon the reaction of the recipient tissues as upon adequacy and distribution of dosage.

Optimal reaction to irradiation is vitiated as much by the poor vascularity of excess scar tissue as by traumatic or inflammatory œdema, so from this viewpoint rapid healing appears highly desirable.

After radical amputation of the breast the healing process is most commonly impaired by collections of blood and serum and sloughing of skin flaps. I believe that these troublesome sequelæ are best avoided by the method of post-operative care to be described. This method is founded upon the simple principles of pressure skin grafting, and by its use skin flaps are made to heal directly to the deeper structures with no more interposed thickness of scar tissue than occurs with a whole thickness or split skin graft.

I have found that the method has the immediate advantage of reducing considerably the period spent in hospital. It also eliminates the difficulties in restoring abduction movements of the arm especially when the incision is not carried laterally over the deltoid muscle. It avoids a subsequent "brawny arm", which is the result of pressure by excess scar tissue upon the axillary vessels.

Principles of Pressure Skin Grafting.

Pressure Thiersch grafting and to a lesser extent split skin grafts cut by the dermatome are generally known and appreciated. With a Thiersch graft a wax mould is used for accurate adaptation and pressure upon a denuded surface; in the split skin method the graft is first sutured accurately to the margins of the area to be covered under normal conditions of elastic skin tension as in a whole thickness graft. In the case of the latter an essential condition for success is that the transplanted whole skin be devoid of fat, and that pressure be continuously and uniformly applied for from ten to fourteen days. The maintenance of the graft's temperature and vitality is assured in the early days only by its raw surfaces being bathed continuously by host serum; and to ensure this no air, clot or serum must be permitted between the opposing surfaces. Movement of the graft must not be allowed to occur.

In most operations for cancer of the breast that I have witnessed some fat is left at the apex of the flaps, and long before the base of the flap is reached muscle is exposed and after this the whole of the subcutaneous fat is reflected with the skin. Perhaps this explains the frequency of local recurrences. The surgeon need not be afraid of reflecting the skin flaps cleanly; he will cure more of his patients and not jeopardize the vitality of his flaps.

Application of these Principles.

An additional requirement for whole thickness skin grafting is the desirability of a firm bed against which to press the graft. The writer has successfully grafted strips of whole skin four inches by two from the loin to the scalp—a bald one. It is fortunate that the chest wall provides just such a firm base. To apply the same principles, the grafts in this instance are envisaged as the skin flaps fashioned at operation for radical amputation of the breast. It may be argued that they receive some blood supply as oozing occurs during scarification of shorter flaps. This supply from the vessels in the flap pedicles is utterly inadequate, and that considerable portions of long skin flaps survive under commonly employed conditions of after-care is due mostly to the unconscious application of pressure for the first day or two when pads and a binder are applied to check post-operative oozing.

How often have we seen flaps look promising for a day, even for a week, only to see them slough progressively in the ensuing days?

The Skin Flaps.

Special attention is given to the skin flaps raised at operation so that no more skin is left than is required just to cover the area. No attempt is made, however, to limit the distance from pedicle to free margin; flap lengths of five inches are common. The incisions required to satisfy the postulates of Halstead are first outlined by scratches made with the reverse side of the knife point. Next, as shown in Figure I, secondary scratches are made to outline those additional portions of skin not needed to cover the area, which will also be removed. And so one removes not only all skin likely to harbour future recurrences, but also such extra skin as is not necessary just to cover the final operation raw area under conditions of

normal elastic skin tension. The only actual incisions made are those finally selected after estimation of both these requirements. I have attempted to illustrate this in Figure I; the area of skin which must be removed to avoid local recurrences is clear, the extra areas which are unnecessary for the covering of raw surfaces and which are removed in addition are shaded.

Another advantage in the removal of surplus skin is that potential spaces for blood and serum accumulation are reduced; even some shock and hæmorrhage may conceivably be avoided by minimizing the amount of skin reflection. An æsthetic advantage, too, is that no œdematous redundant folds of skin remain after healing.

It has already been shown that skin flaps should be devoid of fat.

Of course, especially in those less common cases in which the growth is situated in the inner hemisphere, extreme tension may occur with the suturing of the flaps; here scarification is necessary in order to restore to somewhere near normal the skin tension.

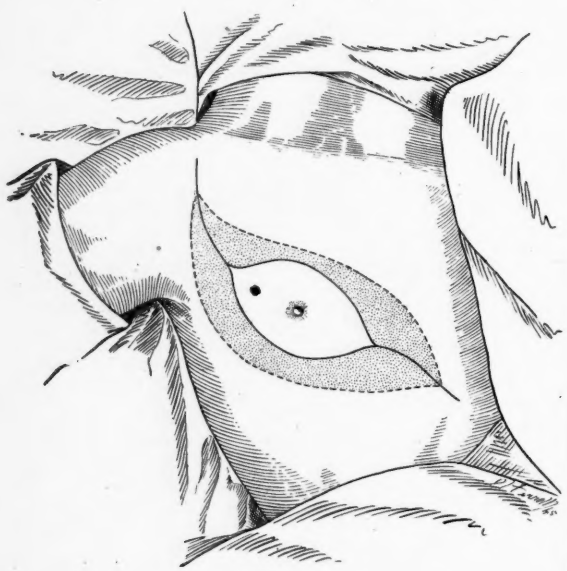

FIGURE I.

In practice serum collects most persistently in the axillary space, and in the inner lower area where there is apt to be an excess of residual skin and where less attention may be paid during the placing of the dressing pads.

The Method.

As the principles of pressure grafting are to be applied, obliteration of space is a prime consideration; and the principal space to be obliterated and the most awkward site for the application of pressure is the axillary space: a "V" shaped gutter running downward, outward, and posteriorly from the clavicle to the posterior axillary fold. This space is consequently dealt with as the primary basis of the method. Four or five thick dressing pads according to the size of the patient (a single special pad, twelve inches wide and four feet in length, would be convenient, but for simplicity in practice no special dressing is asked for) are rolled in cigarette fashion as shown in Figure III, and placed longitudinally to fit firmly into the axillary gutter and to project a couple of inches above the clavicle. Occasionally in the case of outsize patients, and by outsize I refer not only to the obese but the broad shouldered, deep chested type, it is well to place a single rolled pad beneath this as the sulcus may be very deep. In most cases this is unnecessary.

This is the basis of the dressing and all that remains to complete it is to arrange similar but progressively smaller rolls of pads to the inner side of the primary thick axillary roll and shading away in thickness to the mid-sternal line medially. A convenient way of ensuring this is as follows; it is illustrated in Figure III. With a cylinder of five pads as the basic axillary dressing, four pads are rolled into a similar though slightly smaller cylinder which is laid along the inner side of the first, then a smaller cylinder of three pads medial to that again, with a final cylinder of two rolled pads which will be found to reach the midline.

With any other arrangement of dressings I have found it impractical to maintain pressure uniformly over the whole operation area. The rolled pads when compressed flatten against the chest wall and against each other.

A final large pad is placed flat behind and below where the drainage tube emerges, usually at the posterior axillary fold. As it does not cover any part of the operation area it forms no part of the essential pressure dressing, and is used only to absorb immediate post-operative oozing through the drainage tube.

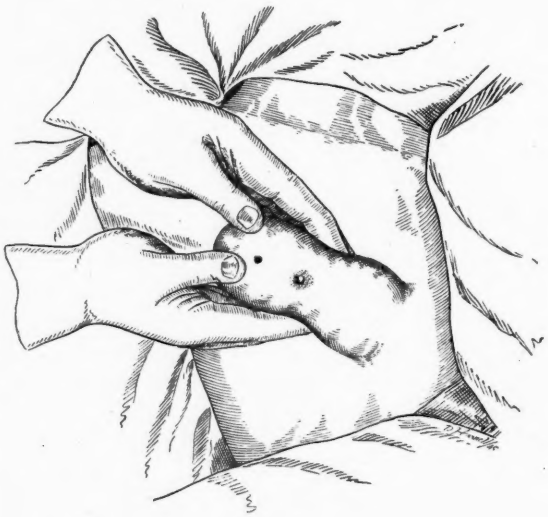

FIGURE II.

A way of estimating the amount of excess skin to be removed.

If any modification of this dressing is tried it can only be advised that the thicker the whole mass of dressing the better; failure will occur only if bulk is avoided.

To obtain pressure a binder is used, a plain affair of strong calico or linen. Flannelette is unsatisfactory: it shreds too readily, especially after laundering. The binder has a width of fourteen inches and is three and a half to four feet in length. With its margin three inches from the midpoint of the binder a shoulder strap of the same material and four inches wide is sewn to the edge of the binder.

The assistant's hand keeps the whole dressing firmly in position while the binder is being drawn tight, during which process there is a strong tendency for the whole dressing to be displaced inward. This is to be guarded against. Standing on the patient's right the surgeon will find that it is convenient to pin the mid part of the binder first and then to pin progressively upward and downward with the pin ends in contact (the long axes of the pins are placed longitudinally). At least five pins will be necessary. The tension used is the greatest which the second and third fingers of the left hand under the binder and the thumb over the binder are capable of maintaining while each safety-pin is inserted. The thumb is apt to

tear through the binder which has been too often to the mechanical laundry.

A practical precaution is to ensure that the upper edge of the binder does not bear too high under either arm; acute discomfort may result and a painful blister develop at this site.

Lastly, the shoulder strap is brought up from the margin of the binder at the back and over the clavicle of the same side, the excess upper two inches of the primary axillary cylinder of dressing is compressed down below the clavicle and the strap is pinned tightly down to the main binder in front with three pins placed in line transversely. The

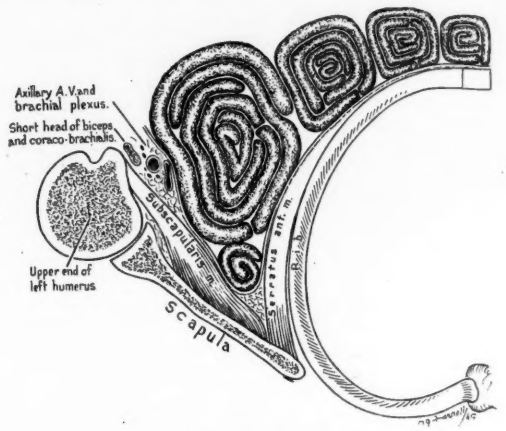

FIGURE III.

lack of rigidity of back and front attachments of the shoulder strap is compensated for by the bunching down of the upper end of the axillary cylinder of dressing, which gives a satisfactory preponderance of bulk below the clavicle and obliterates the upper axillary space.

Instructions are strict: the binder is not to be interfered with by the nursing staff in any way. When oozing soaks through behind where the tube is—it always does—the nurse is instructed to apply a thick pad over the site, to be held with a second binder which can be fitted after her own heart over the original.

Each day the tension of the binder is checked to compensate for stretching or movement, also for any well-meaning ministrations of an elusive night nurse, and it is

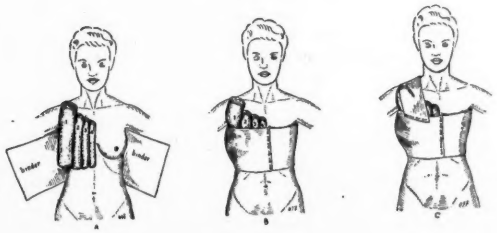

FIGURE IV.

tightened where necessary. Even in large patients only a few pins need to be adjusted in the whole post-operative period; the shoulder strap needs tightening each day or second day. Some patients, in the style of the intelligent horse when being girthed, will learn to take a breath and hold it while the binder is being tightened. This is overcome by awaiting expiration. The compression of the opposite breast causes no discomfort.

The dressing does not tend to slip upward except in the obese; dried blood sticks it to the skin surfaces as effectively as an adhesive, and under conditions of compression the flaps are not nearly so mobile on deeper structures as normal skin.

Most patients bear any discomfort from the tight binder well if the reason for it is explained beforehand; undue discomfort is met by seeking out knotted masses of dressing under the arm which occasionally occur with a restless patient. Only once in three years have I been obliged to give up all attempts at maintaining pressure; it helps if one tells the patient that the binder can be released at any time if she wishes the pressure to be discontinued.

At first dressings were left undisturbed for a week, then for ten days, and finally for two weeks. The last is the ideal period; healing is inevitably slower than in ordinary wounds. In removal the whole mass of dressing is rolled downward, not just dragged off, pressure being maintained with a hand on the dressing immediately below the separating surfaces. The dressing comes away with surprising ease, as dried blood which glues the dressing to skin and wound becomes powdered after the first week.

On removal of the dressings the flaps will be found firmly healed to the whole subjacent surfaces including the

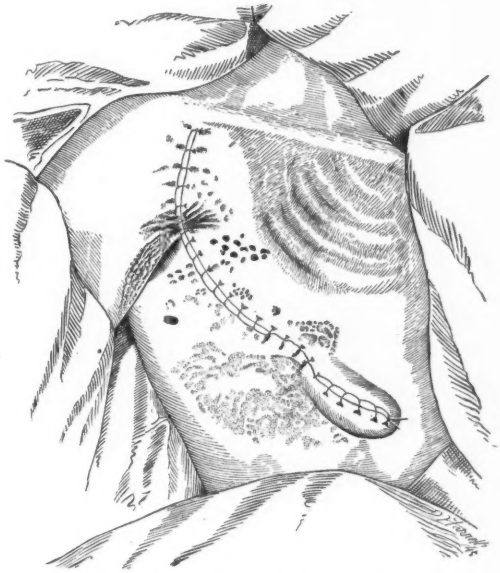

FIGURE V.

Drawing made from an actual patient on the fourteenth day after operation.

axillary vessels and nerve trunks, and with no serum collections; there will be no unsightly areas of puckered skin, though the manner of skin removal is responsible for this latter. No concern need be experienced for any effect pressure may have in compressing vessels in the flap pedicles. This is far outweighed by the grafting result of that pressure.

One would like to say that sloughing will be entirely absent; in the majority of cases it is absent, and healing can be confidently promised in from two to three weeks. When sloughing does occur it involves only an area of half a square inch or so and only part thickness of the skin. This is precisely what is apt to happen along the margins of a free whole thickness pressure skin graft, less often with a split skin graft. Patients are allowed up eight days after operation, while the drainage tube is removed at the first dressing; sutures are removed at the same time, or a couple of days later if the suture line is moist in places.

The arm is not confined to a sling at any time and movements are unrestricted. This does not disturb the bulk of

dressing impacted in the axillary space. Two weeks from the time of operation active abduction of the arm to a right angle can be carried out by all but the most nervous patients. The absence of the usual mass of axillary scar tissue permits of a final normal range of arm movements from the third week, while as mentioned before it also avoids the development of "brawny arm", which I have seen only once in the last three years.

In the immediate post-operative period painful swelling of the arm has occurred in two cases. It was quickly relieved by gently pressing downward the upper margin of hard caked dressings under the upper part of the arm and supporting the limb in slight abduction on two pillows for a day or so.

From a plaster cast of the operation area after healing I have thought of making a single spongy rubber block of the required shape and in three or four sizes to apply over a thin dressing and to take the place of the series of rolled dressing pads. But I am content with the simple method described which gives such good results, and which can be adopted in any circumstances with ordinary everyday dressings.

It may be said: "But I have always used pressure to check oozing, if for no other reason." But it is stressed that meticulous care is taken in the first place to obliterate all space and apply pressure to a reasonable maximum, and moreover to maintain this pressure without disturbing dressings for two weeks. Sepsis does not concern one under present-day conditions. It troubled me in one case in this series, and arose from an infected growth.

The following figures are given to show the period spent in hospital by my own patients after radical amputation, for the years 1944, 1945, and 1946. (In all cases skin flaps were reflected cleanly without fat, the whole *pectoralis major* and delto-pectoral contents were removed, and axillary dissection was carried out by sharp and not by "gauze" dissection.) The number of patients was 54, the average post-operative period in hospital was 27 days.

Summary.

1. A method of after-care in radical amputation for breast cancer is outlined.
2. By application of the principles of pressure grafting the average period of post-operative stay in hospital is 27 days.
3. The method may be expected to result in more favourable reaction of the tissues to post-operative irradiation.
4. It obviates restriction of movements at the shoulder and eliminates "brawny arm".

ARTIFICIAL PNEUMOTHORAX AND INTERNAL PNEUMOLYSIS.[1]

By ALAN KING,
Perth.

HISTORICAL REVIEW.[1][7]

ARTIFICIAL PNEUMOTHORAX was first proposed to rest the "sick lung" by Gilchrist (England) in 1770. James Carson (England) is credited in 1819 with the first animal experimentation and the first definite proposal to apply artificial pneumothorax to the treatment of pulmonary tuberculosis. It was not until 1882 that Carlo Forlanini (Italy) elaborated the principles of artificial pneumothorax and inaugurated this treatment for the human sufferer with pulmonary tuberculosis. Murphy (America) in 1898 further correlated artificial pneumothorax with radiology.

Friedric (Germany) in 1908 first suggested the division of pleural adhesions complicating pneumothorax. He performed open pneumolysis but his results were unsatisfactory. In 1913 Jacobaeus (Sweden) first designed the operation of internal pneumolysis. His double puncture thoracoscope and cautery remain fundamentally the same as those in use today.

From then there has been gradual progress, with increased *tempo* in the last decade, as with the profiting from the experience of many workers, the fundamental principles of collapse therapy, and the place of artificial pneumothorax in this treatment of pulmonary tuberculosis have been established.

PHYSIOLOGY.

Parodi in 1933 expounded some basic concepts which have a very practical application to artificial pneumothorax and internal pneumolysis.[15]

The lung has weight. In man, in the upright position, gravity acts downwards on it. This is modified, of course, by the attachment of the hilum to the mediastinum.

Opposing this during respiration is the force of the expanding movement of the thorax, which is mainly upwards, being due to the intercostal and accessory respiratory muscles. A water manometer, connected to a needle inserted into the pleural cavity, shows a negative pressure swing. The higher of these two levels is, of course, the force of distension and may be called the dynamic level. The lower, which may be called the static level, represents the equilibrium between the weight, or inertia, of the lung on one hand, and the atmospheric pressure and suction effect of the thoracic wall on the other.

In the normal subject in the latero-dorsal position, the reading is $\frac{\text{dynamic}}{\text{static}} = \frac{-6 \text{ centimetres of water}}{-2 \text{ centimetres of water}}$, that is, a ratio of 3:1.

In the pathological picture we have a different and informative reading, and a lessening of the above ratio. The diseased lung is heavier and less elastic; the gravity effect is greater and is opposed by a greater inspiratory force; for example, a reading of

$$\frac{\text{dynamic}}{\text{static}} = \frac{-12 \text{ centimetres of water}}{-6 \text{ centimetres of water}}$$

may be obtained. The presence of pleural adhesions may modify the reading. If these are presumed to be present in the same case as above, a reading of, for example, $\frac{\text{dynamic}}{\text{static}} = \frac{-10 \text{ centimetres of water}}{-7 \text{ centimetres of water}}$ may be obtained—a smaller swing between levels.

The knowledge of these factors is important in relation to artificial pneumothorax and internal pneumolysis. Thus it is possible to interpret the induction and following readings, and to obtain an early indication as to the prognosis of the artificial pneumothorax.

An operation may be performed in two or three stages, use being made of the fact that by controlling the position of the patient between stages, gravity may be employed to stretch an otherwise indivisible adhesion.

ARTIFICIAL PNEUMOTHORAX.

Indications for Artificial Pneumothorax.

Every case of pulmonary tuberculosis remains a clinical entity, but there is now a definite sequence of treatment for the average patient.

A patient with pulmonary tuberculosis is admitted to hospital and undergoes an initial period of bed rest. This period is extremely important. The patient has been recently confronted with his disease, and must be allowed to settle down to his new environment. This initial period must usually cover from three to six months. In many cases of minimal or moderately advanced disease the lesion may heal as a result of bed rest alone.

A proper appreciation of the principles of bed rest is necessary. The problems of mental repose, muscular relaxation, and adequate drainage of the diseased lung must be considered.[16] Collapse therapy now, however, plays a major part in treatment. Between 50% and 60%

[1] Read at a meeting of the Western Australian Branch of the British Medical Association, August 20, 1947.

of patients in any modern tuberculosis hospital now undergo this type of treatment.[11] Cases must be carefully selected; it is of no avail to apply collapse therapy to the patient whose condition is too advanced.

A "complete" artificial pneumothorax is the most satisfactory result as it allows complete healing and fibrosis of the diseased portion of the lung. The aim is "selective collapse" of the diseased area if possible, for example, if only one lobe is affected, collapse of that lobe.

Pneumothorax may be established in only 70% of the cases tried, even when correct indications are followed. Of pneumothoraces established, 70% to 80% may be converted to "complete" collapse, that is to say, after internal pneumolysis if this is necessary.[19] It is advisable to abandon any unsatisfactory pneumothorax and to proceed to a thoracoplasty, if the indications for this operation are also met.[20][21]

Pneumothorax is perhaps a too easily applied procedure. With modern refinements of laboratory technique in culture or guinea-pig inoculation of gastric contents, if sufficient disease is present to warrant a pneumothorax, then sufficient disease is present to allow the demonstration of the causative organism.

Webster[23] has shown the standard which must be attained for any pathological laboratory concerned with the diagnosis of tuberculosis. X-ray diagnosis alone of pulmonary tuberculosis is insufficient.[14] Many conditions—fungous infection, sarcoidosis, atypical pneumonia, lung abscess, bronchiectasis, bronchial carcinoma, and even congestion due to cardiac failure—may mimic pulmonary tuberculosis.

It is important that collapse therapy be not applied during the "exudative" phase of pulmonary tuberculosis. If it is applied, bronchogenic spread occurs, and there is the added risk of tuberculous empyema. Preliminary bed rest usually enables the temperature to subside and diminishes the amount of sputum produced. The "mixed" type of lesion often responds well. At the other extreme, it is not required to apply a pneumothorax to a hard fibrocalcified "productive" lesion.

Indications may be summarized as follows.

Unilateral Involvement.

Pneumothorax is indicated in practically any case of unilateral involvement with or without cavity formation in minimal and moderately advanced lesions providing that the former criteria have been met.

In regard to minimal lesions, this applies to those which have not responded to bed rest and appear to be progressing after, for example, six months' treatment. The moderately advanced lesions must also show lack of, or insufficient response to, bed rest alone.

Advanced lesions may be suitable, but one does not attempt artificial pneumothorax in the presence of large cavitation. "Tension cavities" may be unsuitable,[2][19][22] but a "tension cavity" may change to an ordinary draining cavity, and in time become smaller and suitable for collapse.

Bilateral Involvement.

Pneumothorax is indicated in minimal and moderately advanced bilateral lesions with or without cavity formation in which the disease is preponderant on one side. The collapse is effected on the worse side; the lung with lesser involvement may improve and not need collapse.

Pneumothorax is indicated in moderately advanced disease in which bilateral collapse is planned from the start. The basic rule here is that one side is stabilized first before one proceeds to the other.

Combinations of Collapse Therapy.—Thoracoplasty may be performed on one side with an artificial pneumothorax on the other. Phrenic nerve paralysis is occasionally useful in conjunction with artificial pneumothorax. In some cases there may be fair collapse, but a remaining adhesion to the mediastinum below the apico-mediastinal angle. Elevation of the diaphragm here gives sufficient vertical relaxation, and the affected upper lobe may collapse to a very small volume.

Contraindications to Artificial Pneumothorax.

Possible Contraindications.

Evidence of Previous Pleurisy.—A primary thoracoplasty may be indicated if there is evidence of previous extensive pleurisy and if signs of obliteration, for example, of the costophrenic angle, are present. This is not universal and on occasion an attempt is warranted.

Bronchial Tuberculosis.—If bronchial tuberculosis is extensive, or combined with evidence of stenosis, artificial pneumothorax is best avoided. If it is not extensive, the bronchial lesion may heal subsequently to the healing of the parenchymal lesion.

Extrapulmonary Tuberculosis.—Extrapulmonary tuberculosis may be a contraindication, for example, a tuberculous spine may render it impracticable.

Others.—Any other disease present often decides against artificial pneumothorax treatment, but this is not of universal application; *diabetes mellitus* is an example.

Definite Contraindications.

Extent of Disease.—A giant cavity[7][19] is an obvious contraindication in view of possible complications.

Tuberculous Pneumonia.—Tuberculous pneumonia is a definite contraindication; any collapse immediately converts the lung into an even more solid state and so increases toxæmia. Tuberculous empyema is inevitable.

Silico-tuberculosis.—In the case of silico-tuberculosis there is usually already some respiratory embarrassment, and any increase of this (as would follow pneumothorax) leads to failure of the right side of the heart.

Primary Tuberculosis.—It is not within the scope of this paper to discuss the subject of tuberculosis as a whole, in reference to age *et cetera*, but it is obvious that any primary lesion in the young adult should be left to heal itself; pneumothorax is contraindicated.

Management of Artificial Pneumothorax.

It is important that all refill needles should be sterilized either by autoclave or by boiling. Immersion in spirit or other antispetic is not sufficient. The type of refill needle with the lateral hole, for example, Morlands's is perhaps the best as there is not the likelihood of small pieces of skin or tissue being pushed with a stilette into the pleural cavity. These must be a possible nidus for low-grade infection, so increasing the risk of formation of pleural fluid.

The Kuss needle is perhaps the safest for induction. The usual procedure is to employ local anæsthesia, and if a free pleural swing is obtained, to allow 250 to 300 millilitres of air to be sucked in. This may be followed on the next day by a refill of a similar quantity, after which one day is missed, then two days, then three days, and so on with gradually increasing amounts of air until the pneumothorax is more or less established on weekly refills of 400 to 600 millilitres. Local anæsthesia is not essential except for the first day induction. It is found that the refill time can be gradually extended to two or three weeks and even longer as the artificial pneumothorax progresses.

It is better to avoid large amounts of air and the so-called "concertina" collapse, and rather to have more frequent refills at smaller intervals, with 600 to 800 millilitres as a maximum.

It is a routine to examine every subject by means of the fluoroscopic screen before a refill. It is also now accepted custom to carry on the pneumothorax at a slight negative pressure, for example, −4·0 to −1·0 centimetres of water. "Negative pressure is the most favourable to the attaining of an excellent clinical result free from complications."[7] Positive pressure is no longer justified in the ordinary case[19][20] and is not now employed except in those cases in which an attempt is made to hold an obliterative pleuritis.

It is usual to keep the patient completely at bed rest for six months after establishment of a complete pneumothorax. After a further three to six months of gradually

increasing exercise, the patient is fit for out-patient supervision. Part-time light work may be commenced after three to six months' trial as an out-patient, and this may be followed by full-time work if it is not of an arduous nature.

Duration of Artificial Pneumothorax.

Follow-up surveys have proved that it is necessary to maintain the collapse for many years to prevent relapse of the disease.[19] Minimal disease will require at least three years. Moderately advanced disease requires five years. Advanced disease requires seven years at least.

Complications of Artificial Pneumothorax.

Pleural Fluid.

The commonest complication is the formation of a pleural effusion. This occurs in 50% or more of cases within three to six months after induction, but is generally of no consequence. It may be absorbed or need aspiration.[20] In odd cases it may proceed to tuberculous empyema, but with the selective use of pneumothorax treatment, this should be rare.[21]

Perforation.

Perforation may occur after induction or after a refill. It may be due to the breaking through of underlying disease. In one of three cases of perforation, pleural fluid forms and is generally a mixed or tuberculous empyema.

INTERNAL PNEUMOLYSIS OR ADHESION SECTION.

Whenever an adhesion is present, it must be divided if possible. Adhesions are generally present over a diseased area—perhaps over an underlying cavity. This is the part of the lung at which the selective collapse is aimed.[5][10][17][19] If such adhesions are not divided, there is risk of pleuritis, perforation and empyema, and, at the same time, there can be no guarantee of the healing of the tuberculous process at the base of the adhesion.

It is advisable from the commencement of management of a case that both postero-anterior and lateral films be taken. If the disease is not of the widespread type, it may be possible to localize the affected broncho-pulmonary segment. It is possible to localize a cavity in relation to a certain bronchus.[3] Adhesions may then be forecast at this site.

The commonest site of separate adhesions is in the posterior part of the axilla beside the third or fourth rib, that is, related to the subapical or postero-lateral segment of the upper lobe. Next in frequency are those attached to the cupula of the pleura, under the subclavian vessels, that is, related to the apical segment. I estimate the localization of adhesions approximately as follows: apical segment of the upper lobe, 30%; subapical segment of the upper lobe, 40%; anterior or pectoral segment of the upper lobe, 10%; apical segment of the lower lobe, 10%; other situations, 10%.

Adhesions may be single or multiple bands or veils or fusions.[5] The latter are a result of a more widespread pleuritis.

Adhesions have been classified, notably by Maurer and Sayé,[7][18] but this is perhaps artificial, and one should realize the complete variation possible.

The important facts as regards internal pneumolysis are, firstly, the extent of the adhesion systems, and, secondly, whether lung tissue is present up to the parietal pleura.

The radiological appearance gives much information as to the condition of the adjacent lung, and fluoroscopy may help localization. Tomography may be employed for the same purpose. It is, however, impossible to decide whether a condition is operable or not, except by direct vision, for example, a simple adhesion may be studded with tubercles. Fortunately, thoracoscopy alone is a procedure devoid of risk.[6][19]

Time of Intervention.

The time suitable for intervention is usually from three to five weeks after induction before too much vascularization of the adhesions has occurred.[6][19] The type of disease for which the collapse has been instituted must be considered. It is perhaps advisable to wait longer in the more active type of case.

It is of value that the static pressure reading be approximated to zero for a few days prior to operation, as the patient then supports better the atmospheric pressure in the pleural cavity during operation. (Atmospheric pressure may be represented as any reading with a mean zero, for example, −6+6, −2+2.)

In cases of bilateral pneumothorax, when the second side requires adhesion section, it is of value to allow partial reexpansion of the first side before operation.

Apparatus.

The double puncture thoracoscope is generally employed; one cannula is used for the telescope, and one for the cautery. Single puncture instruments are occasionally used for simple adhesions.

Telescopes have direct vision, or fore-oblique or right-angled vision. Cannulæ may be rigid or flexible. A platinum loop galvano-cautery is employed, four volts alternating current and five to 20 amperes being used; cauteries may be straight, curved or hooked, or articulated-hooks. The articulated-hook of Maxwell may be particularly useful in difficult attachments, for example, to the mediastinum.[12] Curved cauteries through flexible cannulæ often enable an otherwise inaccessible adhesion to be reached. Separate transilluminators, dissectors, hooks, forceps and diathermy electrodes may all be utilized.

Section of adhesion by diathermy electrode is preferred by some workers,[6][10] but is not generally used. It is considered that diathermy causes a spreading zone of coagulation, which, on the visceral end of the adhesion, may lead to later necrosis and perforation. A bipolar electrode has been designed by one operator to minimize this.[13]

Operation.

Local anæsthesia (1% "Novocain" solution) is employed at operation. Premedication may be used in the form of one and a half grains of "Nembutal" one and a half hours before and one-sixth of a grain of morphine three-quarters of an hour before operation.

A planned aproach is necessary. The trained operator generally appreciates the location and type of adhesions.

The patient is placed in the lateral or semi-reclining position, according to the site of the adhesions.

It may be said here that the success or not of the operation depends entirely on the operator, his experience and his method of working.

As most adhesions are apical or posterior axillary, the commonest site for insertion of the first cannula for inspection is in the mid-axillary or anterior axillary line about the fourth or fifth intercostal space. The second cannula may be placed through the pectoral muscle, for example, in the nipple line in the second or third intercostal space. Some operators prefer to reverse this. Each case, however, varies. The second cannula may be placed posteriorly, medial to the scapula, for anterior adhesions. (On odd occasions, a third insertion is necessary.) It is important that the cannulæ be placed more than a hand's breadth apart, to minimize any scissor action of the instruments.

Technique.

Transillumination is the only sure way of determining whether the adhesion contains lung tissue or not. The direct vision telescope (Jacobaeus-Unverricht), in which the globe may be pushed ahead of the lens, allows a simple time-saving way of performing this manœuvre.

The cautery is used at a dull red heat. If it is too dull, it sticks to the adhesion; if too bright, it cuts too rapidly. The adhesion is always cut as close to the parietal pleura as possible.[5][6] Enucleation or disinsertion of large adhesions may be performed after the method of Maurer;[6][12] that is to say, after the edge of an adhesion is cut, a plane of cleavage may be found in

the endothoracic fascia; this may then be sometimes stripped with the cold cautery or a dissector.

Hæmorrhage is usually not a problem during operation. If it comes from small vessels it may be controlled by the heat of the cautery. If this does not control it, local pressure by a small tampon at the end of a forceps may be used. The tampon may be soaked in adrenaline.[5] A diathermy electrode may be used on the parietes; its use is not indicated for a bleeding vessel on the visceral surface.

Termination of Operation.—After the removal of the cannulæ and closure of the wounds, which the use of Michel clips may expedite, the intrapleural pressure is adjusted to that present before operation. The pressure may be left more negative, for example, −6–2, to allow for some reexpansion of the opposite lung. (The latter is considered to have been compressed slightly with movement across of the mediastinum, this being more evident in the long thin type of individual with a flexible mediastinum.)

Complications.

Surgical Emphysema.

Surgical emphysema is minimized by adherence to the above principle of adjustment of intrapleural pressure, and is usually of no consequence. Reasonably firm bandaging by *crêpe* bandages and "Elastoplast" tends to prevent escape of air into the tissues. Post-operative cough control is also essential.

Hæmorrhage.

Hæmorrhage is not a very common complication and is usually controllable during operation, but reactionary hæmorrhage may occur in 1% to 2% of cases.[6][8][10] Occasionally the amount of blood lost may be great enough to require replacement by transfusion, with subsequent aspiration of the pleural cavity. The end result in such cases is generally obliterative pleuritis.

Pleural Effusion.

Simple pleural effusion occurs post-operatively in a percentage of cases. Various authors give different figures for the occurrence of this from 4% to 32%.[6][8][9][10][19] If one is careful during the anæsthetization of the pleura not to squirt "Novocain" into the pleural cavity, and if one is careful during section not to have the cautery too hot, so as to cause charring of tissue and smoke, this complication should not be common. It is possible that the adjustment of the pressure at the end of operation is of definite relation to the post-operative presence or absence of fluid.

Perforation.

Perforation is a rare event, but may occur if lung tissue has been inadvertently cut through. It may occur as a delayed action following necrosis of tissue. It has been suggested that the blood supply may be cut off from an area of the wall of a cavity at the base of an adhesion.[6]

Empyema.

Empyema may follow on simple effusion or perforation. It may be mixed or pure tuberculous. Various figures are given for this complication.[6][10][18][19] Generally it occurs in 1% to 3% of cases. It is obvious that one should not attempt too much, but leave the too difficult case for later thoracoplasty. Technical success in freeing the lung is useless if it is to be followed by such complications.[19]

Conclusion.

Burnet in "The Natural History of Tuberculosis"[4] discusses the apparent failure of current therapeutic methods to influence the course of the disease in the average case and draws attention to the lack of effect of treatment on the mortality rate of pulmonary tuberculosis.

It is suggested that it is only within comparatively recent years that modern methods of collapse therapy have been widely used, especially in Australia; that the place of artificial pneumothorax in the "collapse" treatment of pulmonary tuberculosis is becoming more clearly determined; that artificial pneumothorax is becoming more widely used, but with more selectivity; that results of treatment show a considerable saving of life.[7][9][13]

It is most important to abandon immediately any unsatisfactory pneumothorax and to proceed to thoracoplasty, if the requirements for that operation are also met.

Any apparent failure of therapeutic methods to influence mortality from pulmonary tuberculosis may be due to the fact that there is present always an appreciable reservoir of infection in the community.

At present we are not in a position to give medical care and isolation to all persons with active infective disease. This is due partly to lack of hospital beds, facilities for treatment and trained staff; it is also due in part to lack of specific public health legislation (at least in Western Australia) to make possible isolation of the uncooperative or recalcitrant person who will not conform to the standards of public health required. Such legislation is already in existence elsewhere.[21]

Acknowledgement.

I am indebted to Dr. Linley Henzell for his assistance in the production of this paper.

References.

[1] J. A. Alexander: "The Collapse Therapy of Pulmonary Tuberculosis", 1937.

[2] André Bernou: "The Treatment of Tension Cavities", *The British Journal of Tuberculosis*, Volume XLI, 1947, page 11.

[3] R. C. Brock: "The Anatomy of the Bronchial Tree', 1946.

[4] F. M. Burnet: "The Background of Infectious Diseases", 1946.

[5] H. Morriston Davies: "The Surgical Treatment of Pulmonary Tuberculosis", UNRRA Publication, May, 1945, page 59.

[6] D. Douady and André Meyer: *"Manuel de pleuroscopie et de section de brides"*, 1942.

[7] F. Dumarest: *"Le pratique du pneumothorax thérapeutique"*, 1936.

[8] P. Edwards and A. Lynn: "Closed Intrapleural Pneumolysis", *British Medical Journal*, Volume II, 1939, page 897.

[9] P. Edwards, C. Penman and J. Hogan: "Late Results of Closed Intrapleural Pneumolysis", *British Medical Journal*, Volume II, 1944, page 270.

[10] R. Matson, writing in "Clinical Tuberculosis", by Benjamin Goldberg, 1946.

[11] Personal observations: England, Canada, America, 1945-1946.

[12] R. J. C. Maxwell: "Closed Intrapleural Pneumolysis", *The British Journal of Surgery*, Volume XXVII, 1940, page 527.

[13] R. le P. Muecke: "Internal Pneumolysis During the Conduction of Artificial Pneumothorax Therapy", *Western Australian Clinical Reports*, April, 1940.

[14] J. A. Myers: "The Establishment and Use of Fundamental Procedures in Tuberculosis Control", *Public Health Reports*, Volume LXI, 1946, page 1563.

[15] F. Parodi: *"La mécanique pulmonaire"*, 1933.

[16] W. M. Peck: "The Modalities of Bed Rest", *United States Public Health Reports*, Volume LXI, 1946, page 626.

[17] A. H. Penington: "Pleural Adhesions: Their Effect on and Treatment in an Artificial Pneumothorax", THE MEDICAL JOURNAL OF AUSTRALIA, Volume I, 1947, page 644.

[18] R. Pigeon: *"Coagulation et section des brides pleuro-pulmonaires"*, 1941.

[19] T. N. Rafferty: "Artificial Pneumothorax in Pulmonary Tuberculosis", 1945.

[20] D. B. Rosenthal: "The Incidence of Pleural Effusion in Artificial Pneumothorax", *British Medical Journal*, Volume I, 1936, page 95.

[21] S. J. Shipman: "Pneumothorax versus Apical Thoracoplasty", *American Review of Tuberculosis*, Volume XLV, 1942, page 364.

[22] A. M. Vineberg and W. E. Kunstler: "The Determination and Treatment of Pressure Cavities in Pulmonary Tuberculosis", *Surgery, Gynecology and Obstetrics*, Volume LXXVIII, 1944, page 245.

[23] R. Webster: "Observations Based on Laboratory Experience in Tuberculosis", THE MEDICAL JOURNAL OF AUSTRALIA, Volume I, 1947, page 605.

[24] *The Sanatoria for Consumptives Act*, Revised Statutes of Ontario, 1937, amended to 1943.

STRUMA OVARII ACCOMPANIED BY THYREOTOXICOSIS.

By K. A. McGARRITY and L. F. DODSON,
Sydney.

SINCE Boettlin first described the presence of thyreoid tissue in a dermoid some 57 years ago, about 180 cases have been recorded in which thyreoid tissue was demonstrated in association with either a dermoid or a teratoma. A survey of some of these is given below (Table I), and this serves to demonstrate the variability of the incidence of thyreoid tissue in these tumours according to the investigator. The range covered is 1·5% to 28·5%, with an average incidence of 11·6% in teratomata and dermoids examined by five workers.[1] The above variation apparently depends on the completeness of the examination of the tissue submitted.

TABLE I.

Name.	Teratomata and Dermoids.	With Thyreoid Tissue.	Percentage.
Meigs	27	2	7·4
Pick	21	6	28·5
Rohdenburg	61	9	14·7
Shaw	23	5	21·7
Spencer	66	1	1·5
Totals ..	198	23	11·6

Extensive microscopic studies will often reveal minute areas of thyreoid tissue in many teratomata, and similarly the reverse will occur when the so-called pure ovarian strumata are examined. In the latter, remnants of other germ layers can usually be demonstrated to a greater or lesser degree. Thus the dividing line between a teratoma with some thyreoid tissue and an apparently pure thyreoid tumour of the ovary is somewhat doubtful. But the term *struma ovarii* is used when the greater part of the teratoma is composed of thyreoid tissue.

Out of 180 reported cases of *struma ovarii*, approximately only 5% have been described with accompanying symptoms and signs of thyreotoxicosis which has been directly attributed to the hyperactivity of the gland tissue in the tumour.

Histogenesis.

The histogenesis of these tumours is somewhat obscure; but the suggestion that they were of metastatic origin from an adenomatous or normal cervical thyreoid has been now discarded. Similarly the argument of Bauer that *struma ovarii* is not composed of true thyreoid tissue, but is due to a colloid degeneration of a pseudomucinous cystadenoma, is not tenable, as the tissue shows all the characteristic staining and biochemical reactions of true thyreoid gland (Plant).

It is most probable that the tumour is a one-sided development of thyreoid tissue in a teratoma. In several cases of struma malignant tendencies have been present, and metastases have been described in the omentum, bladder, rectum and liver. Recently a case has been described of a thyreoid-like tumour, resembling a struma, which was removed from the right frontal lobe seven years after an operation for a dermoid cyst of the ovary.[2]

The following case is reported because of the extreme rarity of *struma ovarii* with accompanying thyreotoxicosis.

Clinical Record.

Mrs. F.P., aged fifty-three years, was admitted to Saint Vincent's Hospital, Sydney, on July 7, 1946, because of continuous vaginal hæmorrhage for the last three months following a normal menstrual history up to that time. An examination of the past history of this patient was very interesting. She had been examined and treated four years previously in the out-patient department for pain in the right iliac fossa and right loin. It was recorded in the case notes at that time by her physician that she exhibited signs of exophthalmos, tachycardia (pulse rate 100 per minute) and tremor. On her admission to hospital these symptoms were still present and were combined with pronounced loss of weight (two stone) and nervous apprehension. The pulse rate was irregular, owing to extrasystoles. The degree of exophthalmos was severe. Vaginal examination revealed the presence of a freely mobile cystic swelling in the left side of the pelvis. The uterus was slightly enlarged. The pre-operative diagnosis was *metropathia hæmorrhagica* with a left-sided ovarian cyst.

Operation was performed on July 8, 1946. The left ovary was found to be replaced by a cystic swelling four inches in diameter with a solid area about one and a half inches in diameter at one pole. The cyst had undergone torsion and was twisted twice on the pedicle. The right ovary was small and fibrotic. It was decided to perform panhysterectomy. This was carried out and the patient had a convalescence interrupted by a chest infection. She was discharged from hospital on July 29. Three months later a great improvement had taken place. The patient had gained over two stone in weight. The pulse rate had slowed to below 80 per minute and the pulse was now quite regular. Nervous symptoms had completely disappeared and the exophthalmos was considerably reduced. The blood pressure had fallen slightly, and previous symptoms of palpitations had vanished. Succeeding examinations since that time have revealed a continuation of the improvement over and above that usually demonstrated after such an operation.

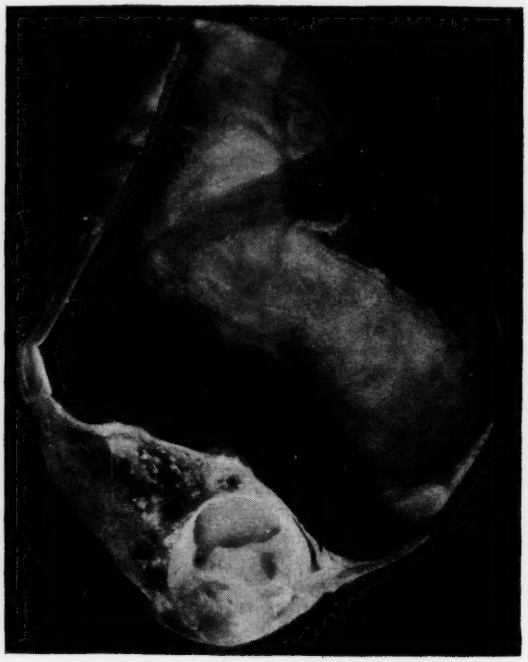

FIGURE I.
Bisection of cyst and thickening in its wall.

Pathological Report.

The pathological examination of the specimen removed at operation revealed the following findings. It was a spheroidal cyst nine centimetres in diameter, mainly translucent, but with a darker solid area four centimetres in

diameter, which could be seen and felt at one pole. The exterior was smooth, an open network of fine vessels being visible on the wall. Examination of a section through the diameter at the solid area revealed a unilocular cyst with a smooth interior, from which watery straw-coloured fluid escaped. The solid area was now seen to be a lens-shaped thickening in the wall (which was elsewhere thin and fibrous), about three centimetres wide in its thickest part. The cut surface of the solid area presented a variegated appearance. On one side it was soft, semi-translucent and flecked with bright yellow spots. On the other side numerous small cysts varying in size from a pin's head to a pea were present and contained translucent jelly-like material resembling thyreoid colloid (see Figure I).

Microscopic Appearances.

Numerous blocks were cut from the solid nodule in the cyst wall at various levels. The predominant tissue was thyreoid. In one block only other teratomatous elements were found. The thyreoid tissue bore a close histological resemblance to one of the common adenomata of the gland. Examination of this tissue showed many large and small acini lined by low cuboidal epithelium. The acini contained colloid material deeply stained with eosin and reaching to the free margin of the lining cells, the colloid showing clefts but no peripheral vacuolation (see Figure II).

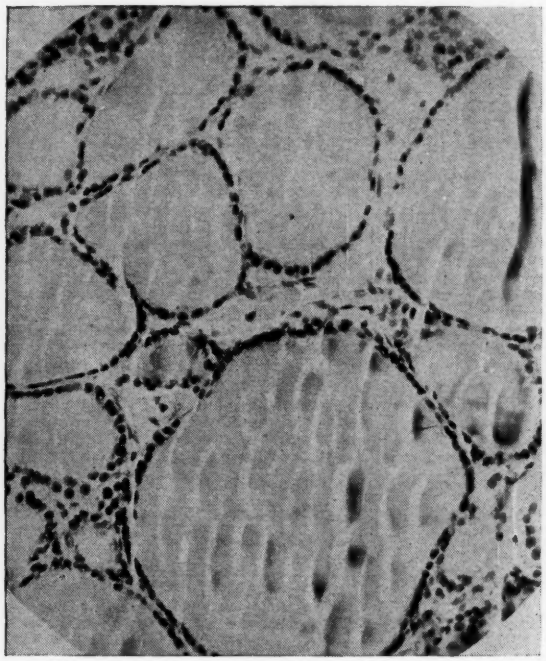

FIGURE II.

Thyreoid tissue present in tumour showing an area with large acini filled by colloid.

In other areas the alveoli were small, closely packed and lined by cubical cells, and contained pale colloid. Interspersed with these were cord and columns of thyreoid cells, frequently with only minute lumina or else none at all (see Figure III).

Only a few alveoli were lined with tall columnar cells, and these often showed papillary projections into a lumen filled with pale and vacuolated colloid. The stroma was frequently hyaline, structureless and faintly eosinophilic, and marked here and there with hæmorrhages from thin-walled capillaries. Other areas showed typical spindle-celled ovarian stroma.

Scattered in the stroma were groups of rounded or polygonal cells with small central nuclei and pale or slaty granular cytoplasm. Many of these groups abutted on and formed a cuff about some of the thyreoid alveoli. The cyst wall was composed of compressed ovarian stroma and fibrous tissue with an outer endothelial lining and an inner epithelium of flattened or cuboidal cells.

In one recess the cells were tall columnar with basal nuclei, and although they were not definitely goblet cells, they bore a close resemblance to those found in a pseudo-mucinous cystadenoma (see Figure IV).

Discussion.

This case presents all the features, both clinical and histological, consistent with a *struma ovarii* which has produced symptoms and signs of thyreotoxicosis. The possible origin of these toxic manifestations from the ovarian tumour was discovered only after the microscopic examination had been made. The correlation was confirmed later by rapid disappearance of the toxic symptoms and by the continued clinical improvement. Yet the microscopic appearances of the thyreoid tissue were not consistent with the clinical degree of thyreotoxicosis. This latter inconsistency has been noted in most of those other similar conditions described in the literature.

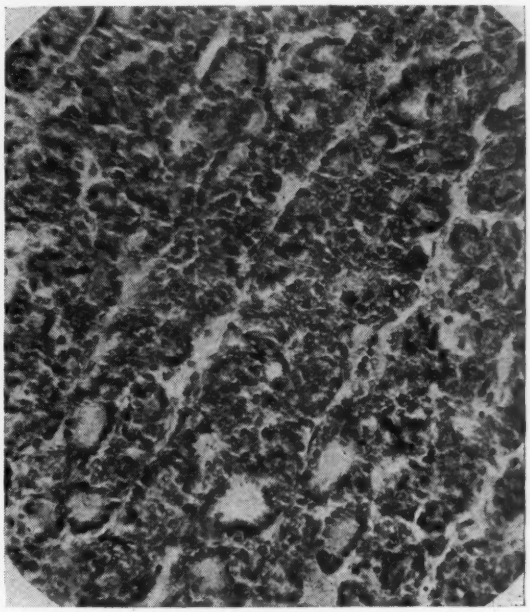

FIGURE III.

An area of thyreoid tissue present in tumour showing small closely packed acini resembling "fœtal thyreoid".

Moench, Kovacs and Kleine, in association with five other separate workers, have described *struma ovarii* with toxic manifestations which cleared up on removal of the tumour.[3][4] In each of these cases the microscopic evidence of hyperplasia was not parallel with the severity of the toxic symptoms. In some of these cases, in which full biochemical data were available to establish the nature of the disease beyond doubt when taken in conjunction with the clinical state, none of the microscopic stigmata of hyperthyreoidism were present. Yet in all of them the removal of the tumour was followed by immediate amelioration of symptoms. It would therefore appear reasonable to consider the ovarian struma as a functioning part of the total thyreoid tissue of the body, which may react to iodine lack or to the thyreotropic hormone or to any other stimuli in a manner similar to the thyreoid itself.[5]

Moench describes a case in which the severe toxic symptoms are associated with an ovarian cyst containing only a piece of thyreoid tissue of almost microscopic dimensions contained in the cyst wall.[6]

Gusberg and Danforth and Hundley describe two cases in which thyreoidectomy was performed without relief of symptoms. Later removal of a *struma ovarii* was immediately successful in relieving the condition.[5][7]

Summary.

1. A case of *struma ovarii* causing symptoms of thyreotoxicosis is described with photomicrographs and pathological findings.

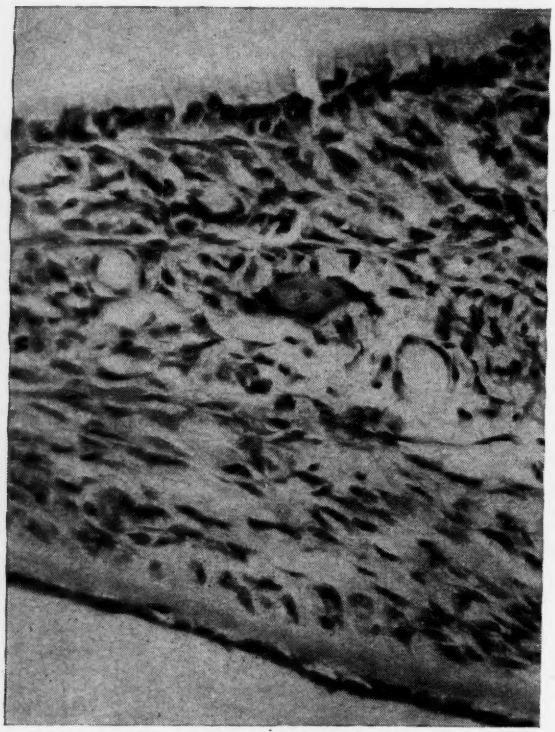

FIGURE IV.

Cyst wall. Centrally is the compressed ovarian stroma; to the right is the flattened epithelium, which lined most areas, and to the left is the tall columnar-celled epithelium, which lined one recess in the cyst wall.

2. A short survey of the histogenesis of *struma ovarii* is given.

3. A dissection of some reported series of teratomata and dermoids is given, showing the incidence of thyreoid tissue to be approximately 11·6%.

4. The incidence of toxic symptoms with *struma ovarii* is shown to be between 4% and 5% in 180 cases reported.

5. The histological evidence of hyperplasia in these reported cases does not parallel the degree of thyreotoxicosis produced by the tumour.

Acknowledgements.

We wish to express our thanks to Dr. Donovan Foy and Dr. A. H. Tebbutt for their assistance in the preparation of this case report.

References.

(1) H. M. M. Wynne, J. S. McCartney and J. F. McClendon: "Struma Ovarii", *American Journal of Obstetrics and Gynecology*, Volume XXXIX, 1940, page 264.

(2) E. Novak: "Gynecological and Obstetrical Pathology, with Clinical and Endocrine Relations", Second Edition, 1947, page 432.

(3) L. de Bakey, junior, and F. de Lehocyhy: "Cerebral Metastases of Ovarian Struma", *Confinia neurologica*, Number 1, 1944, page 22, and *Obstetrical and Gynecological Survey*, Volume I, 1946, page 266.

(4) L. A. Emge: "Functional and Gross Characteristics of Struma Ovarii", *American Journal of Obstetrics and Gynecology*, Volume XL, 1940, page 740.

(5) S. D. Gusberg and D. M. Danforth: "Clinical Significance of Struma Ovarii", *American Journal of Obstetrics and Gynecology*, Volume XLVIII, 1944, page 540.

(6) G. L. Moench: "Thyroid Tissue Tumors of the Ovary", *Surgery, Gynecology and Obstetrics*, Volume XLIX, 1929, page 150.

(7) J. M. Hundley: *American Journal of Obstetrics and Gynecology*, Volume XL, 1940, page 749.

Reviews.

CLINICAL LABORATORY METHODS.

THE purpose of "Notes on Clinical Laboratory Methods" by the Standing Committee on Laboratory Methods, University of Glasgow, is to secure uniformity of the laboratory methods employed in the clinical teaching at Glasgow.[1] Apart from this special purpose for which it is designed, this small volume of 95 pages, with 16 blank pages for notes, should provide a useful book for the medical student, and one which he can carry with him quite conveniently. It presents time-tested methods for performing the simpler laboratory investigations, though a few tests are included which need more elaborate apparatus and a more involved technique, and these are marked with an asterisk. All the tests are described simply, clearly and succinctly, and average findings in health are tabulated at the end of each of the chapters. Useful information, not always easy of access elsewhere, is also included on the collection and transmission of specimens for pathological examination. A noticeable omission is a technique for the quantitative estimation of the total proteins in the cerebro-spinal fluid; nor is there any mention of the qualitative estimation of glucose in the cerebro-spinal fluid, an estimation which usually forms part of the routine examination of this fluid.

The book, however, is written for a special purpose, and despite any omissions, presumably the result of set purpose by the committee, the book should be beside the student when he is called upon to perform side room testing as part of his clinical examination of the patient.

THE PHYSIOLOGY OF WOMAN.

IN "Woman Unknown", a small book by George Grange,[2] an attempt is made to provide the lay person with an account of the normal physiological processes of woman. The author found that there was no suitable publication available when he was asked for information on this subject by his patients.

His general approach to the subject is perhaps more satisfactory than the technical details. He first outlines the structure and purpose of woman in relation to her functions in society. He emphasizes the many problems that have arisen in recent times through woman attempting a way of life at variance with her make-up.

There are deficiencies, as in the variations in normality, and errors, as in the causation of morning sickness, in such a book because of the impossibility of covering a large subject in a small publication. Generally, the description of parenthood, menstruation, pregnancy, puberty and the menopause is satisfactory. It would have been improved by several simple diagrams, as the lay person may not understand the detail of structure outlined. Also a little more detail in the management of the various phases would give the book more practical value.

The most impressive feature of the book is the delightful and adequate way in which it stresses the purpose and place of woman in society, and until this is appreciated many of the ills which beset us will continue.

[1] "Notes on Clinical Laboratory Methods", by the Standing Committee on Laboratory Methods, University of Glasgow; Fifth Edition revised; 1947. Glasgow: John Smith and Son (Glasgow), Limited. 7¼" × 5", pp. 96. Price: 3s. 6d.

[2] "Woman Unknown", by George Grange, M.B., B.S.; 1947. Sydney and London: Angus and Robertson. 7¼" × 5", pp. 118. Price: 5s.

The Medical Journal of Australia

SATURDAY, JANUARY 10, 1948.

All articles submitted for publication in this journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations and not to underline either words or phrases.

References to articles and books should be carefully checked. In a reference the following information should be given without abbreviation: initials of author, surname of author, full title of article, name of journal, volume, full date (month, day and year), number of the first page of the article. If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

THE FEDERAL COUNCIL: A PLEA FOR ACTION.

IT would be illuminating to read some of the papers if medical practitioners were called upon from time to time to sit for written examinations on matters associated with their general activities. Among the questions that would be set would appear before long: "What do you know about the British Medical Association and its activities?" Never can we forget the indignation of a senior member of one of the Branches who fulminated against the Federal Council that one could not expect much from it, seeing that so many of its members were departmental medical officers, heads of health departments. This man has taken an active part in the affairs of the Association and he could not distinguish between the Federal Council and the National Health and Medical Research Council. In these circumstances it may be pardonable to remind readers that the British Medical Association has two main objectives — the promotion of the medical and allied sciences and the maintenance of the honour and interests of the members of the medical profession. As pointed out on many previous occasions in these columns, there is significance in the order in which these two objectives are placed, and it cannot too often be insisted that the main object of the Association is to increase the sum of knowledge about the human and animal body and the diseases which may affect man. There are several ways in which the objects of the Association may be attained. These include the holding of meetings, the publication of information in the journal of the Association, the occasional publication of transactions, reports and other papers, the granting of sums of money for the promotion of the medical and allied sciences (witness the recent announcement from the Parent Body about the awarding of scholarships and prizes), and "such other lawful things as are incidental or conducive to the attainment of the above objects". Every year scientific papers are read at the annual meeting of the Association and medico-political matters are discussed at the Annual Representative Meeting (the "A.R.M."), which is the parliament of the Association. In addition to its usual, or what we may call its set, activities, the Association has from time to time appointed special committees to investigate and report on special matters. Reports have appeared on such subjects as abortion, medical education, fractures, immunization, psycho-analysis, mental deficiency, miners' nystagmus, nutrition and physical education. At the present time a committee of the Association is investigating the question of medical education in Great Britain.

The activities of the British Medical Association in Australia comprise those of the six Australian Branches and all matters affecting the profession as a whole are the concern of the Federal Council. The activities of the Branches reflect in general those of the whole Association. The scientific work of the Branches is given prominence at their monthly Branch meetings, and most of the papers read at these meetings, with the remarks made in discussion, are published in this journal. From time to time meetings with a medico-political bearing are held, but these are much less numerous than the scientific gatherings. Most of the medico-political matters are dealt with at council meetings and many of them are matters almost of routine. When the medico-political matters have an Australia-wide significance they are considered by the Federal Council. It would, however, be a mistake to suppose that the Federal Council has no concern for scientific matters, those which, as has been emphasized, are the chief object of the whole Association. The Federal Council is responsible for, and controls, the holding of the sessions of the Australasian Medical Congress. Prior to the formation of the Federal Committee (the forerunner of the Federal Council) the congresses were held in different States at intervals of a few years, and the Government of the State in which they were held gave some assistance in the matter of finance; the continuance of the sessions was in actual fact almost wholly dependent on the life of one man—the man appointed at one session to act as president when congress met again. The congresses had no part in British Medical Association organization. About ten years elapsed after the formation of the Federal Committee before the congresses passed, as it was logical that they should, into the control of the British Medical Association. All this may seem like a digression, but it is intended to show that the Federal Council is not a body charged solely with an oversight in matters medico-political. That a great deal, indeed most, of the time of the Federal Council has latterly been given over to medico-political matters has been inevitable and is the result of government action. There is a danger that in the urgency of present discussions the duty of the Federal Council in other matters may be overlooked. This would be a pity, because the Federal Council is the only body that can speak and act for the whole profession in the Commonwealth of Australia; if it should fail to take the lead other bodies will step in and do the work that it should do.

There are two matters which are of the greatest importance to medical practice, both now and in the future. They have been causing a good deal of concern in other parts of the English-speaking world, and Australia will have to deal with them sooner or later. These are medical education and the recruitment of nurses. In the issue of July 19, 1947, we discussed at some length the General Medical Council of Great Britain and its attitude to medical education. Its recommendations on the medical

curriculum were published *in extenso*. Reference was also made in the issue of November 15, 1947, to medical education in the United States of America and Canada. In the issue of November 29, 1947, attention was drawn to a report on the recruitment and training of nurses, published by the Ministry of Health, and it was described as demanding the careful attention of all who have to do with the control of nursing in Australia. Reference to these three discussions in our columns will at least give some idea of the magnitude and urgency of the problems. Though they concern the practice of medicine in all countries, no one will deny that they have special aspects, complicated by Australian conditions, for which a solution will have to be found in Australia. Australia cannot sit back and wait until Britain or Canada or America has solved a problem from the British, Canadian or American point of view and apply the solution to its own needs. Even if it could do so, it would not be a praiseworthy attitude to adopt. The Federal Council, if it is to take its rightful place as the agent and mouthpiece, the leader, of the medical profession in this country, should do something to set going an inquiry into both these problems from the Australian point of view. That this will not be easy is at once obvious. The distances between States make meetings of committees difficult; but the difficulties should not be insuperable. Though suggestions might be put forward in regard to the kind of inquiry that should be made in each instance, how it should be made, and by whom, this will not be done. Rather would we bring the two subjects mentioned to the notice of the Federal Council in the hope that it will take the statesmanlike action that it is well qualified to take.

Current Comment.

COLLAPSE FOLLOWING EXERTION.

AFTER an illness, whether of medical or surgical nature, or under conditions of great fatigue, transitory syncopal signs are not uncommon. These, however, are not so striking as those instances of collapse occurring in healthy and well-trained persons after exertion. In competitive sport these episodes are perhaps more frequent than in less dramatic circumstances, which is not surprising, for the nervous factor of strain cannot be disregarded, and there is also more likelihood of the subject's demanding of himself the outpouring of every available ounce of energy. But there is a physiological side to this condition which is intrinsically interesting, quite apart from the aspects which concern the spectators of sporting events and the readers of the daily Press. Some fifteen years ago the underlying circulatory phenomena were first studied, and since then researches into aviation medicine have directed inquiry along cognate and more important lines. L. W. Eichna, S. M. Horvath and W. B. Bean have recently published a study carried out on healthy young American soldiers who were undergoing some specialized phase of military training beyond the ordinary basic training.[1]

They applied tests to these men under standard conditions, in which they carried packs of one-third their own body weight, ran on a motor-driven treadmill and undertook long hikes at a relatively fast rate. The postural responses after exercise were then studied with a tilt-table, exercise tests were applied, and also mental tests involving simple calculations in a limited time, and cold pressor tests. Three types of response were observed, which the authors term the syncopal, the abnormal and the normal. The men who showed signs of syncope usually had low blood pressures and rapid hearts, but collapse was the most striking feature. They felt drowsy, yet apprehensive, nauseated and giddy, and in the more severely affected consciousness was more or less disturbed or even lost, and vomiting or loss of visual function occurred. The usual concomitants of collapse, such as sweating, pallor, cyanosis, and gasping respiration, in addition to fall in blood pressure and increase in heart rate were observed. These phenomena were induced by the erect position and relieved by the supine position, though a transitory bradycardia was common when this change of posture was made. The men classed in the abnormal group showed objectively an unusual fall in systolic blood pressure and in many cases both objective and subjective signs and symptoms of collapse occurred also, but these were not severe, and did not prevent the men from standing erect for the required period of five minutes. In the normal group no deviations from the usual standards of response to the tests were found. The authors have made an extensive analysis of the material gathered by this research, and found that orthostatic hypotension occurred in about half the healthy young men they tested when subjected to vigorous exercise involving the lower extremities. The results were the same after prolonged exertion and brief severe effort. Half of the men showing hypotension manifested syncope. They found that those manœuvres which moved blood out of the lower extremities or prevented the pooling of blood there relieved the hypotension. It is of interest that the fall in blood pressure often was quite persistent, and did not disappear until an hour or more after the cessation of exertion. The mechanism of the hypotension and syncope is believed by the authors to be a pooling of blood in the vascular beds of the lower limbs, where dilatation of the vessels must occur. It is suggested that the reason for this is a failure of the muscular venopressor mechanism in the legs, associated with a reduction in muscular tone. This factor is thought to be more important than a mere dilatation of blood channels. The authors did not include in their investigations tests of the sensitivity of the carotid sinus mechanism, though it would seem worthwhile to follow up the work of Weiss and others in this direction. It does not seem possible to forecast from previous observations of healthy men which of them are likely to be subject to syncopal disturbances following severe exertion. If some simple method of determining this tendency could be devised it would have many useful applications; but our experience with physiological studies on the results of exertion on bodily functions would rather make us doubt if the medical examiner can ever be the complete prophet either in military physical efficiency or in sport. It is perhaps regrettable that the name "*Die Sportkrankheit*" was given to this striking type of response to heavy exertion in the earlier German literature, for it is not a disease. Further studies on the subject would be interesting, and should help to consign to oblivion the tenets of a former day when the rapid and temporarily overacting heart after effort was unfortunately labelled "athlete's heart".

[1] *The American Journal of the Medical Sciences*, June, 1947.

REVOLT FROM THE BEDPAN.

RECENTLY there has been a revival of interest in the shortening of convalescence of patients in hospitals, particularly with regard to what has been described as the early mobilization of the bed patient. There has also been spirited argument over the use of aperients during the period of recovery after surgical operations, even in the presence of acknowledged abdominal sepsis. It is curious, too, that the introduction of anti-coagulants such as heparin and "Dicumarol" has stimulated the use of early movement as a prophylactic against the rare though all too serious hazards of post-operative thrombosis. The whole subject is really bound up with a review of nursing methods, and in this connexion it should be remembered that, although nurses as a class are very conservative,

it is from doctors that they originally receive their doctrines, and if change is necessary the responsibility is in the latter's hands.

G. Bohmansson and H. Malmros, writing as chief surgeon and physician in a Swedish hospital, have condemned the bedpan and the enema.[1] Their revolt against the enema in general we need not discuss, as it is hoped that this method is reserved in modern practice for real necessity only. But surely it is time that more consideration was given to the patient's comfort in an unsatisfactory method of dealing with the function of evacuation which involves an unnatural and unphysiological posture, namely the use of the bedpan. It may be conceded that some such appliance is necessary for patients who must maintain the recumbent posture, but it does seem rather absurd that patients such as woman soon after delivery are encouraged to move and to take abdominal exercises and yet expected to use a method of defæcation which is uncomfortable and inefficient. Bohmansson and Malmros describe a wheel chair which can transport all patients who can be lifted or helped on to a seat so that the toilet can be used in the normal way without further disturbance. They state that this device has proved very popular with both patients and nursing staff, and has come into use in most Swedish hospitals. One difficulty can be seen in this country at least, that the method might prove a greater strain on depleted staffs, and might perhaps need more generous sanitary arrangements in hospital wards. But it may seriously be questioned if this problem has been considered with the care that it really demands: it has even happened that the use of commodes in a ward has been forbidden, although experienced nurses advised it in the interests of patients. In the planning of a house the details and location of the sanitary conveniences are given careful attention: similarly a change in hospital methods in this regard might affect hospital planning also, but this is no argument against an attempt at improvement in the routines of nursing procedure. Even without radical changes it is surely possible to add to the comfort of those bed patients who can move without pain or risk, and to speed their convalescence and lessen its hazards.

WAR WOUNDS OF THE HEAD.

As a permanent tribute to the work of British surgeons in the war of 1939-1945 and as a means of enabling them to record their experiences, *The British Journal of Surgery* is preparing a series of four special supplements on war surgery. The first of these, which deals with the treatment of wounds of the head, has now been issued[2] and must be regarded as a most valuable contribution to medical literature.

In a foreword G. E. Gask points out that the war of 1939-1945 was the first in which Britain had had an effective organization for the segregation and treatment of patients with wounds of the head. The results were impressive and convincing. An outstanding feature of the organization was the creation of mobile neurosurgical units which were raised and trained at the parent hospital in Oxford and made available when and where the circumstances of war indicated. Much of the supplement is made up of the reports by the commanders of these units, detailed records of fine work performed under widely varying conditions. Likely to be of most interest in this country are the reports relating to North Africa and to Burma. Gask quotes the instance of a mobile unit which was sent forward with the Eighth Army across Cyrenaica, Tripolitania, and Tunisia, and, with the aid of air evacuation, maintained a head injury service over a distance of 2000 miles from front to base. "Most of the head wounds were operated on within twenty-four hours of wounding, a remarkable achievement, and in consequence the incidence of brain sepsis fell and the rate of primary healing increased." He goes on to stress the primary importance of good surgery in the results obtained, a fact supported by many contributors to the supplement. However, it is of great interest to read a discussion by Geoffrey Jefferson in which he compares the facts relating to head wounds and infection in the two World Wars. He describes from first-hand experience the development of neurosurgery during the war of 1914-1918; notable results were certainly obtained, but infection and slowness of recovery were great problems. The surgeons of that time learnt through bitter experience that "the aseptic surgical ritual" did not apply without qualification to battlefield surgery and, when they looked for the ideal antiseptic, found that it did not exist. Valuable discoveries were later made in antisepsis, but Jefferson quotes with approval Fleming's statement in 1919: "All the great successes of primary wound treatment have been due to efficient surgery, and it seems a pity that the surgeon should wish to share his glory with a chemical antiseptic of more than doubtful utility." As Jefferson remarks, this is as true today as it was when it was written; "it is not surgery which has altered, it is the antiseptics". Jefferson quotes the work of such neurosurgeons as Whitaker and Harvey Cushing whose surgery was sound, but who were repeatedly defeated by infection, especially that not accessible to surface antiseptics. In the 1939-1945 war penicillin radically altered this situation; infection was controlled and, as an important corollary, it was possible to close head wounds with all the consequent advantages. The development of plastic surgery helped to overcome the mechanical difficulties of wound closure after excision of scalp tissue. Jefferson divides his praise for the successful treatment of head wounds in the 1939-1945 war between the young neurosurgeons and those who were responsible for developing penicillin.

It is not possible to make further reference to the vast amount of material presented in the rest of the supplement. There are reports by surgeons at the base hospitals and by commanders of mobile neurosurgical units; special aspects, such as the bacteriology of wounds, receive individual attention; there is an admirable atlas of operative technique with 65 illustrations, nearly all in colour; a general outline of the development and work of the neurosurgical service is contributed by Hugh Cairns from the British Army's aspect and by Lambert Rogers from that of the Royal Navy. It is pleasing to see that Gask in his foreword designates, as the "inspiration and driving force" in the fine wartime achievements described, the Consulting Surgeon in Neurosurgery, Sir Hugh Cairns, together with his band of brilliant young surgeons. Cairns, a truly distinguished Australian, will be visiting this country during 1948. It is appropriate here to refer to his answer to the question often asked during the war by medical men and military commanders as to whether this work was worth while and whether the men with their head and spinal injuries would not be better dead. He points out the number of cases in which completely successful treatment allowed early return of the soldier to duty and asserts that the results after more severe penetrating wounds cannot be foretold.

> There are undoubtedly a few with brain wounds whose lives become so miserable that it would have been better had they died. But, as Cushing said, there is no tribunal on earth which can decide that treatment should be withheld from this or that patient. It would be the negation of progress to withhold it.

War surgery and talk about it are out of fashion just now, but it is well that these supplements should present what has been done before the memory of it has become stale. It is fitting, as Jefferson remarks, that the army surgeons should have "the opportunity to set down their experiences and conclusions for posterity (which the philosophers tell us begins now) to read". It is certainly right that the developments which can be applied to civilian surgery should be known and appreciated, but devoutly to be desired that the military aspects should be of historical interest only.

[1] *The Lancet*, October 4, 1947.
[2] *The British Journal of Surgery*, War Surgery Supplement Number 1: "Wounds of the Head."

Abstracts from Medical Literature.

GYNÆCOLOGY.

Diverticulitis of the Colon in Gynæcology.

EDWARD ALLEN AND L. BRUCE DONALDSON (*The Western Journal of Surgery, Obstetrics and Gynecology*, July, 1947) review 59 cases of diverticulitis of the colon occurring in patients treated by members of the gynæcological staff of the Presbyterian Hospital of Chicago. The average age of the patients was fifty-two years, most being in the age group forty to sixty years. Left lower quadrant abdominal pain occurred in 49 patients, the next most common symptoms being backache (24 patients), belching, flatulence and distension (27 cases), bladder disturbances (24 cases), chronic constipation (26 cases), and diarrhœa and fever (24 cases). The pelvic finding characteristic of the disease is described as an indurated, nodular, "lava-like", tender mass, fixed high in the left side of the pelvis and often pulling the uterus to the left. Movement of the cervix or body of the uterus may cause pain. Chronic perforation of an infected diverticulum may produce a pelvic abscess. Pelvic examination was carried out on 51 of the 59 patients; the findings were given as normal pelvis (fourteen cases), diverticulitis of the colon (ten cases), inflammatory mass (three cases), pelvic inflammatory disease (eight cases), ovarian cyst (five cases), uterine fibroids (eight cases) and pregnancy (three cases, two of which were thought to be tubal). Carcinoma of the bowel was thought to be the existing pathological condition in seven cases; this diagnosis may be difficult to deny by means of X-ray examination after a barium enema and also by gross inspection on the operating table. Nineteen of the 59 patients were subjected to laparotomy, and the authors consider twelve of these operations were unnecessary procedures. Four patients underwent posterior colpotomy for drainage of pelvic abscesses; each one of these required repeated drainage and two developed fistulæ. Surgical intervention or radium therapy may lead to adhesions and intestinal obstruction, fistulæ, abscess formation and peritonitis.

Carcinoma of the Uterine Cervix.

WILLIAM P. GIVEN (*American Journal of Obstetrics and Gynecology*, June, 1947) presents an analysis of facts concerning 212 patients with carcinoma of the uterine cervix, of whom 115 have been followed for at least five years. The majority of patients were almost equally represented in the fourth, fifth and sixth decades of age; nine patients were under thirty years of age and ten patients were over seventy years of age. The analysis shows that 86% of patients had borne children. Approximately 74% of patients had symptoms for six months or less, but 10% had no symptoms. The incidence of adenocarcinoma of the cervix was 7·9%, and cancer of the cervical stump was present in 3·8%. Two patients in the series had cancer of the cervix complicating pregnancy and in two other patients cancer of the cervix was discovered four or five weeks *post partum*. There was no apparent correlation between histological classification and survival rate, but clinical classification was of great prognostic significance. Approximately two-thirds of the patients were classified as having lesions in Stages I and II. For treatment 80% of all patients were given X irradiation followed by radium therapy after an interval of one month. Late radiation reactions occurred in 22% of patients, the most common complications being cystitis and proctitis. Infection during the course of irradiation is by far the most important complication associated with radiotherapy of cancer of the cervix. The 2% mortality charged against this procedure is considered due to the activation of hæmolytic streptococci by radiation. The overall five-year survival rate among 115 patients was 42·5%, and all but five of these patients were classified as having lesions in Stage I or Stage II. A patient classified as having a Stage I or Stage II growth has a 60% chance of surviving five years, whereas a classification of having a Stage III or Stage IV growth offers a hopeless prognosis beyond this period. Careful inspection of the cervix in all patients and the free use of biopsy cannot be overemphasized. In every instance where the cervix is diseased and a total hysterectomy can be performed safely, such a procedure should be undertaken. Prophylactic chemotherapy should be instituted in all cases prior to irradiation treatment when cultures of hæmolytic streptococci have been grown from routine vaginal swabbings.

Absorption of Penicillin from the Vagina.

MORRIS A. GOLDBERGER, ROBERT I. WALTER AND LOUIS S. LAPID (*American Journal of Obstetrics and Gynecology*, March, 1947) report the blood levels and urinary excretion of penicillin after the administration of single large doses by the vaginal route in the form of pessaries. The study was carried out on ten patients who were free from vaginal or cervical infection. After a vaginal douche of sterile water five suppositories of calcium penicillin in a base of cocoa butter were inserted into the vagina at one time. Each suppository contained 100,000 units of penicillin. In each patient the pH of the vagina was determined before and after treatment, the blood penicillin level was estimated, and the urinary excretion was noted for twenty-four hours. After the intravaginal administration of 500,000 Oxford units the average penicillin level in the blood was 0·38 unit per millilitre of serum at the end of half an hour, 1·35 units per millilitre at the end of one hour, 0·96 unit per millilitre at the end of two hours, and 0·38 unit per millilitre at the end of three hours. The total urinary excretion of penicillin in twenty-four hours varied between 33,425 units and 142,000 units, the average being 91,957 units. It is evident from these observations that penicillin is readily absorbed from the vaginal mucosa and appears in the blood in high therapeutic levels. The method of treatment is painless, the suppositories are well tolerated and can be administered by the patients themselves. No untoward local or systemic toxic effects were observed. Absorption from the vagina was found to be somewhat slower and more prolonged than absorption after intramuscular injection. This method warrants clinical trial and may prove to be the method of choice for the administration of penicillin to the adult female.

Radium Treatment of Cancer of the Cervix Uteri.

R. G. MALIPHANT (*The Journal of Obstetrics and Gynæcology of the British Empire*, April, 1947) has reviewed 837 cases of women with cancer of the *cervix uteri* who were treated with radium. On assessing results it was found that the five-year "cure" rate was the most useful, but 15% of women surviving five years died during the next five-year period and 6% of those surviving ten years subsequently died of cancer. The deduction of 15% from the three-year survival rates for the fourth and fifth years provides a valuable index to the probable five-year end-results. The material was classified on the basis of cell structure into three morphological groups—the adult, ripe or spinal cell type, the plexiform mid-ripe or transitional cell type, and the unripe, anaplastic spindle-cell type. There was no relation found between the age and parity of the patient and the cellular type of the carcinoma. In general the cell structure did not influence the naked eye appearance, but more than half of the adenocarcinomata appeared as hypertrophic growths, while the spindle-cell cancers were much less commonly seen in this form. Of the tumours 95·7% were squamous-cell carcinomata, and the final result among these improved slightly but significantly with the degree of anaplasia of the growth. In the small group of adenocarcinomata (4·3%) results of treatment were not satisfactory. The hypertrophic fungating cancers showed a much better five-year result than the ulcerative type, irrespective of the degree of advancement. The duration of the symptoms was a poor index to the extent of the disease and therefore to the prognosis; but the presence of pain, although not invariably indicating advanced disease, had an adverse influence on the prognosis. The absolute survival rate among 585 cases treated by the "two-application" Stockholm technique was 25·2%.

The Influence of Semen on the Female Reproductive Organs.

V. B. GREEN-ARMYTAGE, F. SILBERSTEIN AND G. E. WACHTEL (*The Journal of Obstetrics and Gynæcology of the British Empire*, June, 1947) report experimental results of human semen and homologous semen injected into immature animals in order to determine whether the absorption of semen produced any effect on the genital organs. Experiments were based on the clinical observation that the uterus and upper third of the vagina in many young virginal women were abnormally small, but such uteri grew to their accredited normal size within a few months of married life provided no contraceptives were used which interfered with the absorption of semen from the vagina. Previous experiments with the injection of heterologous semen into rats and rabbits suggested the production of a considerable effect on the female genitalia. Fourteen experiments were carried out on spayed mature rabbits and similarly spayed litter mates were used as controls. It was found that the atrophic changes in the uterine

wall which follow castration were prevented by injections of human semen. In order to determine whether injected semen exerted any progestational activity on the uterus, the effects of semen injection into spayed rabbits primed with stilbœstrol was studied. No difference was noted between the does which had received stilbœstrol only and those which after stilbœstrol treatment had been injected with human semen. Heat inactivates semen, and further experiments suggested that the effect of semen injected is entirely, or at least partly, due to one or more factors which are insoluble in acetone but soluble in benzene. Insemination would appear to be the ideal method of reproducing physiological conditions, but it is beset with difficulties in rodent animal experiments. Experiments on the intravenous injection into rabbits of homologous semen showed definite effects on the reproductive organs. Follicle stimulation and precocious development of the uterus were noted. In spayed does such injections not only prevented atrophic changes after castration, but produced hypertrophy. Experiments on unspayed animals were carried out in which one ovary and one uterine horn were removed twenty-four hours before injections of semen were given. Twenty-four to thirty-six hours after the last injection of fresh semen the does were killed and the remaining ovary and uterine horn were removed and compared with the ones removed before the experiment. In twelve such experiments three animals showed no effects following semen injections, and six showed generalized follicular stimulation. All the uterine horns removed after injections showed a considerable increase in length, and in some experiments the horns had increased in width. The variety of ovarian and uterine changes following the injection of semen suggests that the results depend not only on the nature of the injected semen but also on the phase of the receptor organ, and that simultaneous hormonal influences from the ovaries, the pituitary and the adrenals must be considered.

OBSTETRICS.

Puerperal Gynæcology.

JACOB L. BUBIS (*American Journal of Obstetrics and Gynecology*, May, 1947) reports his experiences over thirty years in gynæcological plastic and repair operations performed immediately after deliver for new, old or combined birth injuries. The author and his colleagues at Mount Sinai Hospital have practised and advocated this form of treatment since 1918, and he finds it difficult to understand why the principle has not been more generally adopted in view of the good results and standardized technique. This form of treatment should be carried out only by the trained gynæcologist. Surgical procedures involving the birth canal after delivery have been considered dangerous on account of the risks of sepsis and hæmorrhage, but operations in which careful technique is combined with strict asepsis are not followed by these complications. The author considers that any obstetrician who is also a gynæcologist can form judgement as to whether relaxation of the pelvic floor will be temporary or permanent, and so it is possible to anticipate prolapse and to perform a prophylactic repair operation. The repair of cystocele, rectocele or perineum, and the cure of new or old lacerations of the cervix is more practical, more efficient and more economical immediately after childbirth than a later operation to cure a long-standing disability. The contention that the lochia interferes with healing of the tissues has been disproved. Following gynæplastic repairs the maternal morbidity has decreased from 23·5% in 1922-1929 to 4% in 1936-1946. It is stated that the mortality and morbidity rates have been lower than those reported by institutions in which no gynæplastic operations were performed during the puerperium. The author claims that there is a great saving of time and money and that the mother has improved general health, prophylaxis against subsequent disabilities, and probably some protection against cancer.

Failure of Müllerian Duct Fusion.

STANLEY WAY (*The Journal of Obstetrics and Gynæcology of the British Empire*, August, 1947) reports a further 19 cases in which there were minor degrees of failure of fusion of the Müllerian ducts; this, combined with a previous series of 18 patients, gives a total of 37 patients who had in all 78 pregnancies. Anatomically, there were 31 cases of *uterus bicornis unicorpus unicollis*, five cases of *uterus subseptus*, and one case of an unclassified condition. In 27% of pregnancies (21 pregnancies) there was a transverse position of the fœtus; in 26% (19 pregnancies) abortion occurred; in 15% (12 pregnancies) the placenta was retained; breech and premature labour each occurred in 9% (7 pregnancies); whilst *placenta prævia* and prolapse of the cord each occurred in 5% (4 pregnancies). In the third stage postpartum hæmorrhage was frequent and occurred nine times in sixteen cases of labour. The author states that women with this deformity, which can be recognized antenatally, should be delivered in hospital. There is a suggestion, too, that the deformity may be inherited as the stillborn offspring of one of the mothers had a *uterus bicornis unicorpus unicollis*, two of the reported cases were in sisters, and in one case it was likely that the patient's mother and elder sister also had the deformity.

Fibroid Tumours in Pregnancy.

FROM 1934 to 1945, 122 cases of fibroids in pregnancy were recorded at the University College Hospital, London, or an incidence of 0·79%, according to E. W. C. Buckell (*The Journal of Obstetrics and Gynæcology of the British Empire*, February, 1947). Of the cases 25 (or 20·5%) occurred in *primigravidæ* of thirty-six years of age or more. After the exclusion of those with toxæmia and malpresentation, only 49 patients (40%) had normal pregnancies, (12 (9·8%) threatened to abort, and 17 (14%) miscarried; ten of the miscarriages occurred after the third month. On ten occasions premature labour occurred and six of these infants were lost. Premature interruption of pregnancy therefore occurred in the case of 27 out of 122 patients (22·1%). Red degeneration was observed in 22 patients (18%), at times from the commencement of gestation to term; in all cases except two the patients were treated conservatively, and in the two exceptions myomectomy during the twelfth and thirteenth week did not disturb the pregnancy. Five cases of ante-partum hæmorrhage occurred, for which a cause could not be found. Myomectomy was attempted only five times—twice for red degeneration, twice for the mistaken diagnosis of ovarian cysts, and once for a large fibroid which was considered a possible obstruction to labour; one patient aborted following operation and one bled so copiously that hysterotomy was performed. Hysterectomy was performed on six patients with a previable fœtus—in four the pregnancy had not been diagnosed. Of the 88 patients who came into labour, eight (9·1%) had primary uterine inertia; four of the latter were delivered by Cæsarean section; eleven infants were extracted with forceps. Twenty-two patients were delivered by Cæsarean section—an incidence of 25%. Only two patients had a post-partum hæmorrhage. Seven patients had a morbid puerperium, but in only two could this be attributed to fibroids. Three patients died—one from shock following Cæsarean section, one from ileus following Cæsarean section and myomectomy, and one from bronchopneumonia complicated by vesicovaginal fistula and sloughing fibroids following craniotomy. The fœtal and neonatal death rate was 11·1%; 79 patients out of 113 had healthy children.

"Avertin" and Eclampsia.

J. B. DEWAR AND W. I. C. MORRIS (*The Journal of Obstetrics and Gynæcology of the British Empire*, August, 1947) present the results of the rectal administration of "Avertin" in 44 cases of eclampsia. The initial dosage given was 0·425 millilitre per kilogram of body weight made up to a 3% solution at 40° C. This can be repeated in three hours if necessary and then again in three hours, to produce twenty-four hours' sedation. No serious difficulties were encountered in the administration, and with the dosage employed there was no clinical evidence of liver damage or any undesirable side effects other than bronchitis. The only instance of contraindication in the series was in relation to a patient whose eclampsia was complicated by concealed accidental hæmorrhage with much shock. The obstetric management was artificial rupture of the membranes following the first dose of "Avertin", when the finger could be passed through the cervical canal. With an unfavourable cervix, artificial rupture of the membranes was avoided in mild states for twenty-four to forty-eight hours after the crisis had passed; in severe states Cæsarean section was considered, and, if performed, was carried out under "Avertin" and local anæsthesia. The maternal mortality in the series was 4·5% (two deaths) compared with a rate of 20·5% (eighteen deaths) among 88 eclamptic patients otherwise managed. Once treatment was commenced, only three patients had a recurrence of fits, and only one of these had more than one fit. The patients became quiet within twenty minutes; the colour remained good; there was no vomiting; a sharp fall in blood pressure was invariably noted. The normal course of labour was not effected. There were 15 fœtal deaths (or 30·6%) compared with 34 (or 41·5%) among the patients otherwise managed. The authors attribute no neonatal death to the method of sedation.

Bibliography of Scientific and Industrial Reports.[1]

THE RESULTS OF WAR-TIME RESEARCH.

During the war a great deal of research was carried out under the auspices of the Allied Governments. It has been decided to release for general use a large proportion of the results of this research, together with information taken from former enemy countries as a form of reparations. With this end in view, the United States Department of Commerce, through its Publication Board, is making a weekly issue of abstracts of reports in the form of a "Bibliography of Scientific and Industrial Reports". This bibliography is now being received in Australia, and relevant extracts are reproduced hereunder.

Copies of the original reports may be obtained in two ways: (a) Microfilm or photostat copies may be purchased from the United States through the Council for Scientific and Industrial Research Information Service. Those desiring to avail themselves of this service should send the Australian equivalent of the net quoted United States price to the Council for Scientific and Industrial Research Information Service, 425, St. Kilda Road, Melbourne, S.C.2, and quote the PB number, author's name, and the subject of the abstract. All other charges will be borne by the Council for Scientific and Industrial Research. (b) The reports referenced with an E number may be obtained in approved cases without cost on application to the Secondary Industries Division of the Ministry of Post-War Reconstruction, Wentworth House, 203, Collins Street, Melbourne, C.1. Copies of these are available for reference in public libraries.

Further information on subjects covered in the reports and kindred subjects may be obtained by approaching the Council for Scientific and Industrial Research Information Service, the Secondary Industries Division of the Ministry of Post-War Reconstruction, or the Munitions Supply Laboratories (Technical Information Section), Maribyrnong, Victoria.

PB M 60923. ETSTEN, B., *et alii.* Pentothal anæsthesia: Physiological basis. January, 1947. 2 pp. Price: Microfilm, $1.00; Photostat, $1.00.

This is a short summary of a film which was used for a motion picture demonstration. The film is a record of patients receiving 1% "Pentothal Sodium" intravenously. The signs of "Pentothal" anæsthesia progressing down the neuraxis are mentioned as well as the technique for the determination of the cerebral metabolic rate from blood samples.

PB M 63278. FLEISCHMANN, WALTER, AND BRECKLER, ALFRED. Mitotic activity and wound healing in the corneal epithelium of rats treated with thiouracil. No date. 1 p. Price: Microfilm, $1.00; Photostat, $1.00.

Mitotic counts in flat preparations of corneæ of rats treated with thiouracil were compared with those of littermate controls. The number of mitoses as estimated from the colchicine experiments was significantly reduced in the rats treated with thiouracil. In the experiments without colchicine the counts were not reduced in the rats treated with thiouracil. According to the present abstract, this indicates that not only the onset of mitosis, but the duration of the mitotic cycle, is slowed down in thiouracil-treated rats. Superficial wounds of the cornea heal in the same time in hypothyreoid rats as in normal controls.

PB M 50331. WENDT, G. R., AND TUTTLE, A. D. Studies in motion sickness. Series B. (CAA Div. of Res. Rept. 60.) April, 1946. 78 pp. Price: Microfilm, $2.00; Photostat, $6.00.

This is the continuation of work reported earlier (see PB 50313) and consists of three papers: (1) "Frequency of susceptibility to motion sickness among young adults." A series of *questionnaire* surveys was made with seven groups of college students and a group of airline stewardesses. The results have been presented for normative purposes. Questions concerning susceptibility at various age levels showed the greatest frequency at the grade school ages. Women reported more motion sickness than men. (2) "Airsickness among 189 airline stewardesses and its relationship to previous history of motion sickness." The frequency of airsickness was: 42% had vomited from airsickness, 36% had experienced lesser degrees of sickness, 22% had been completely free of sickness. History of sickness on other devices yields some useful prediction of airsickness. (3) "Airsickness among 71 student pilots and 15 instructors and its relationship to previous history of motion sickness." The percentage frequency of airsickness was: vomiting—students 16, instructors 20; lesser sickness—students 52, instructors 67; not sick—students 32, instructors 13. The correlation of motion sickness inventory score and airsickness category was 0·73 in the case of student pilots and 0·34 in the case of instructors.

PB M 63802. GUTMANN, HELMUT R., *et alii.* The role of methylene blue and pyridine nucleotides in the reduction of methæmoglobin in hæmolyzates. No date. 1 p. Price: Microfilm, $1.00; Photostat, $1.00.

In the absence of added substrates, methylene blue oxidizes hæmoglobin in washed intact and laked erythrocytes according to this abstract. Also in the presence of glucose or lactate and methylene blue, methæmoglobin is reduced in intact methæmoglobinæmic cells, but not in water hemolyzates prepared therefrom. Conditions are defined for the action of methylene blue as an oxidant of hæmoglobin or as a reductant of methæmoglobin. The abstract resulted from work done for the Medical Division, Edgewood Arsenal, Maryland.

PB M 63830. HORTON, R. G., *et alii.* Conversion of –CN to –CNS in dogs. No date. 1 p. Price: Microfilm, $1.00; Photostat, $1.00.

This report compared briefly the –CN and –CNS content of hepatic vein blood and femoral artery and vein blood subsequent to the injection of LD50 doses of sodium cyanide into the femoral vein of dogs. Determinations of –CN and –CNS were made by the Aldridge-Evans methods. It was considered likely that some –CN disappears without prior conversion to –CNS, as, for example, through the lungs. This document, which appears to be an abstract of a report, is a contribution from the Medical Division, Edgewood Arsenal, Maryland.

PB M 53063. BLACK, SIMON, AND THOMSON, JOHN F. Some metabolic effects produced by large doses of DI-β-chlorethyl sulphide in rats. No date. 15 pp. Price: Microfilm, $1.00; Photostat, $1.00.

This study was carried out at the University of Chicago Toxicity Laboratory and the Department of Pharmacology to determine whether a very large dose of mustard gas could produce *in vivo* effects which might be related to its inhibitory effects on the carbohydrate metabolism *in vitro*. The dose employed caused normal adult rats to die two to three hours after poisoning. Analyses of blood and plasma showed a picture typical of severe anoxia. Perfusion experiments done on the hindquarters of normal and poisoned rats to determine other than anoxic effects are not conclusive. Only lactic acid formation was about 25% less in the poisoned tissue. Three tables and a bibliography of eleven items are attached.

PB M 60706. BRYSON, VERNON, AND SWANSTROM, MARYDA. Immunization of mice against pneumococcal pneumonia by inhaled polysaccharide. No date. 2 pp. Price: Microfilm, $1.00; Photostat, $1.00.

This study was conducted at the Biological Laboratory, Cold Spring Harbour, New York. Sixty mice were exposed to aerosolized polysaccharide. Six days after the final exposure all animals, including twenty controls, were injected intraperitoneally with pneumococci suspended in sterile broth. Total polysaccharide dispensed and estimated individual dose inhaled can be correlated with mortality. Immunity against pneumococcal infection by exposure to polysaccharide aerosol has been produced in some animals.

PB M 60380. BRYSON, V., *et alii.* Problems of aerosol therapy with special reference to the calibration of dosage, and antibacterial synergism. Final report. November, 1946. 53 pp. Price: Microfilm, $2.00; Photostat, $4.00.

This study was conducted at the Biological Laboratory, Cold Spring Harbour, New York. The programme of investigation dealt with: (1) Calibration of procedures in use at Edgewood Arsenal and the Western Pennsylvania Hospital, Pittsburg, Penna., for the administration of penicillin aerosols to experimental animals. (Conferences on methods, experimental pneumococcal pneumonia in mice.) (2) Development of a method for the measurement of aerosols absorbed into the blood stream when administered by inhalation. (Survey of possible methods, use of phenolsulphonphthalein in man, measurement of aersols absorbed into the blood stream in animals.) (3) Determination of possible additive effects of administration of penicillin, when administered by inhalation of aerosols and concurrently by other routes. (Calculation of total aerosol dosage in mice, experimental results, discussion and conclusions, radio-active sodium chloride as an aerosol.) (4) A study of the biological effects of aerosols of penicillin, other antibiotics and chemotherapeutic agents administered with and without detergents

[1] Supplied by the Information Service of the Council for Scientific and Industrial Research.

or other synergistic substances; with and without agents intended to delay absorption; in normal animals and in animals with experimental pneumonia. (In-vitro studies of antibacterial synergism, in-vivo studies of antibacterial synergism.)

PB M 48863. COMROE, JULIUS H., JUNIOR, AND BOTELHO, STELLA. The unreliability of cyanosis in the recognition of arterial anoxæmia. No date. 22 pp. Price: Microfilm, $1.00; Photostat, $2.00.

This work was performed in the Department of Physiology and Pharmacology, Graduate School of Medicine, and the Departments of Surgical Research (Anæsthesia) and Pharmacology, School of Medicine, University of Pennsylvania. Serious arterial anoxæmia may exist before even moderate cyanosis is visible. Diagnosticians differ widely in their ability to recognize visually the presence of arterial anoxæmia. The development of the oximeter by Milliken made it possible to study large numbers of observers and subjects. It was seen that the detection of cyanosis depends not only upon variables in the patient, but also upon variables in observers to note colour changes, and that cyanosis is a poor guide for the detection of arterial anoxæmia of slight to moderate degree. Serious grades of arterial anoxæmia may be unrecognized by many physicians unless arterial blood is obtained and analysed for oxygen content and capacity. Two tables and a bibliography of eight items are attached.

PB M 51045. CRESCITELLI, FREDERICK, AND GILMAN, ALFRED. Electrical manifestations of the cerebellum and cerebral cortex following DDT administration in cats and monkeys. No date. 18 pp. Price: Microfilm, $1.00; Photostat, $2.00.

This work was carried out at the Section of Pharmacology, Medical Research Laboratory Medical Division, Chemical Warfare Service, Edgewood Arsenal, Maryland. Following the intravenous administration of DDT emulsions into 24 cats and 13 monkeys which had previously been treated with small doses of sodium pentobarbital to suppress the convulsive action of DDT, the following alterations occurred in the spontaneous electrical potentials recorded from either the exposed or non-exposed cerebral cortex and cerebellum: (i) The cerebellar rhythm progressively increased in magnitude. (ii) The activity from the cortex increased slightly in magnitude and in frequency. In non-anæsthetized, curarized cats and monkeys characteristic periodic electrical manifestations were recorded from the cerebral cortex and cerebellum following the administration of DDT. Prior to the initial electrical seizure, fast waves appeared in the electrograms. These waves increased in magnitude and frequency of occurrence until eventually periodic electrical seizures appeared in both the motor cortex and cerebellum. These seizures were in general similar to the electrical pattern in *grand mal* epilepsy in humans.

PB M 53070. DUBOIS, KENNETH P., *et alii*. Studies on the mechanism of action of thiourea and related compounds. III. The effects of acute poisoning on carbohydrate metabolism. No date. 22 pp. Price: Microfilm, $1.00; Photostat, $2.00.

In continuation of work carried out previously at the University of Chicago Toxicity Laboratory and the Department of Pharmacology, University of Chicago, it was found that acute poisoning by ANTU, phenylthiourea, allylthiourea and thiourea results in hyperglycæmia in rats. Higher quantities of ANTU were necessary to produce hyperglycæmia in guinea-pigs than in rats. Lethal doses of the above drugs produced a marked drop in liver glycogen in rats. Other experiments dealt with the antagonizing action of insulin, ergotamine and adrenaldemedullation, the effect of hypophysectomy, epinephrine content of blood *et cetera*. A bibliography of fifteen items and four graphs are attached.

PB M 40334. EVANS, ROBLEY D. Argon desaturation. Monthly progress report, No. 1-3, bound with development of technique for measuring saturation and desaturation curves by the use of long-period radioactive argon at atmospheric pressure, and abstract of final report, Mass. Institute of Technology, OEMcmr-392, by R. D. Evans *et alii*, August, 1944. (National Research Council Committee on Aviation Medicine Report 347.) December, 1943, to April, 1944. 6 pp. Price: Microfilm, $1.00; Photostat, $1.00.

Two new apparatus for use in making continuous measurements of the radioactive content of exhaled breath were developed. Both include Geiger-Muller counters which operate satisfactorily while containing a moving stream of moist gas at atmospheric pressure. They may be used with long-lived radioactive argon, or any other radioactive gas. They can be used in quantitative studies of the transport of gases across the active surface of the human lung. Thus it is possible to take data on the saturation and desaturation of the entire body, using a variety of gases. The extent of lung damage and the progress of healing following lung injury by blast, toxic agents, or œdema from other causes, might be evaluated quantitatively. These reports cover work performed under OSRD Contract M-3553.

PB M 49647. FARLY, ROBERT L., AND MORGAN, HERBERT R. Studies on the chemotherapy of viruses in the psittacosis-lymphogranuloma group. IV. Effect of certain chemotherapeutic agents of psittacosis virus (6BC strain) infections in mice. November, 1945. 19 pp. Price: Microfilm, $1.00; Photostat, $2.00.

Eighteen mice were infected by way of the intravenous, intraperitoneal, intracerebral or respiratory routes with broth dilutions of yolksac suspensions containing a known amount of virus. Therapy was begun either by subcutaneous injection of the drug in saline solution or by oral administration. The effects of the following drugs were studied: sodium sulphadiazine, penicillin, streptomycin, and *p*-aminobenzoic acid.

PB M 40331. FAIR, GORDON M. Disinfection of vegetables and fruit contaminated with *Entamœba histolytica* cysts. Abstract of interim report No. 3. (OSRD Committee on Medical Research, Tropical Disease Report 46, Abstract.) January, 1945. 1 p. Price: Microfilm, $1.00; Photostat, $1.00.

Instructions are given for the application of "Mikroklene" that was used in the field for the disinfection of mess utensils. One unit of fresh "Mikroklene" in fourteen gallons is cysticidal at all temperatures normally encountered if the food is soaked for thirty minutes. "Ceepryn" is both cysticidal and detergent in concentrations of 50 parts per million for 30 minutes in both clear and polluted water over a wide range of temperature. "Bursoline No. 3" is effective in concentrations of about 105 parts per million in ten minutes (fifteen tablets per quart) at the resulting pH of 5·0.

PB M 49645. GEE, LYNN L., AND GERHARDT, PHILIPP. *Brucella suis* in aerated broth culture. II. Aeration studies. September, 1947. 27 pp. Price: Microfilm, $1.00; Photostat, $2.00.

Employment of a reciprocating shaker apparatus provided an optimum, yet constant and easily reproducible, rate of air supply for broth cultures of *Brucella suis*. This technique was used as a standard reference procedure. Aeration requirements for maximum growth of the organism in sparger aeration systems were interdependent upon two factors: type of sparger and the antifoam agent necessary to control foaming. The viable all count generation time was used as an index of aeration requirements. Employment of a gradually increasing aeration rate gave approximately the same yields as a constant high aeration rate and enhanced the control of foaming in the early stages of growth of sparger aerated cultures. One diagram, two graphs and eight tables are attached.

PB M 49646. GERHARDT, PHILIPP. *Brucella suis* in aerated broth culture. III. Continuous culture studies. September, 1945. 19 pp. Price: Microfilm, $1.00; Photostat, $2.00.

So-called "cyclic" continuous culture systems were constructed and operated, in which addition of fresh medium and withdrawal of culture were made at periodic intervals, a portion of the product being retained as starter for the ensuing cycle. A laboratory scale apparatus was developed in which addition of fresh medium and withdrawal of products were accomplished continuously and simultaneously and by which a *Brucella suis* suspension of very high concentration, uniformity and purity was produced. A bibliography of eight items, one diagram and five tables are attached.

PB M 49644. GERHARDT, PHILIPP, AND GEE, LYNN L. *Brucella suis* in aerated broth culture. I. Preliminary studies on growth assays, inoculum, and growth characteristics in an improved medium. September, 1945. 24 pp. Price: Microfilm, $1.00; Photostat, $2.00.

Techniques for the determination of light transmittance, catalase activity, oxidation reduction potential, pH, and plate count in broth cultures of *Brucella suis* were surveyed and modified. Statistical analyses were made of important assays. Growth curves were established for shaker cultures in fortified tryptose broth, using concurrent evaluations of the assays. One photograph, five graphs and three tables are attached.

PB M 40461. GIBBS, FREDERIC A. Electroencephalographic selection of air force personnel. Abstract of final report. (OSRD CMR Neuropsychiatry Report I, Abstract.) January, 1944. 1 p. Price: Microfilm, $1.00; Photostat, 1.00.

The standard electroencephalograph, being useful for screening against epilepsy, requires too much expert interpretation to be used as a general test for candidates for flying instruction. A simplified procedure was tried, but its value is questioned. This report covers work performed under OSRD Contract OEM cmr-167. For progress reports see PB 40462.

British Medical Association News.

SCIENTIFIC.

A MEETING of the Victorian Branch of the British Medical Association was held at the Royal Melbourne Hospital on August 20, 1947. The meeting took the form of a series of clinical demonstrations by members of the honorary medical staff of the hospital. Part of this report appeared in the issue of January 3, 1948.

Supradiaphragmatic Vagotomy.

DR. E. E. DUNLOP presented a patient who had undergone supradiaphragmatic vagotomy for chronic duodenal ulcer with intractable pain. The patient, a male, aged sixty-four years, had had symptoms for over twenty years, and one perforation. Pain had become exceptionally severe and was unrelieved by medical treatment in hospital. Features of the condition were a high degree of acidity, absence of stenosis, and a rapidly emptying stomach. The continuous secretion (twelve hours' nocturnal secretion) was over 1000 millilitres and gastric motility was high. Supradiaphragmatic vagotomy had been carried out on August 13, 1946, under cyclopropane anæsthesia with controlled respiration; resection of the eighth rib on the left side was performed. All vagal strands were resected from the root of the lung to the diaphragm.

When the patient's condition was reviewed one year later it was noted that the relief of pain which was instantaneous had been sustained with no dietetic restriction. The continuous gastric secretion under similar conditions was reduced to 300 millilitres, and hyperchlorhydria was replaced by sustained achlorhydria. Only during the last month had acid secretion approached normal values. Tracings revealed greatly reduced gastric motility with no response to insulin hypoglycæmia. X-ray examination after a barium meal revealed a marked delay in gastric emptying from which slow recovery was occurring. The duodenal cap was still deformed, but no crater was demonstrable. The complications of the operation were mild post-operative distension, and diarrhœa which still persisted to the extent of four motions daily. That might be related to hypochlorhydria. The patient was actively working and enjoying a full range of diet and was very pleased with his condition.

Dr. Dunlop stressed the fact that the operation was still on trial. It might prove of value in chronic intractable conditions with high acidity and absence of stenosis. A stenosing ulcer was a definite contraindication to its use.

Polyposis of the Small Intestine.

Dr. Dunlop's second patient, a girl, aged nineteen years, had had multiple adenomatous polypi of the small intestine and duodenum associated with recurrent intussusception and treated by a double bowel resection including the duodeno-jejunal flexure and portion of the duodenum. The symptoms were colicky abdominal pain and vomiting for several years. A sausage-shaped tumour had been noted on several occasions. One year previously an intussusception of the ileum had been reduced and an adenomatous polypus removed at the Women's Hospital. At operation on December 13, 1946, intussusception was noted to be present at two sites of multiple polypoid masses, the first in the ileum, and the second about the duodeno-jejunal flexure. Both regions were resected and in addition the bowel was opened and a polypus removed from the mid-gut zone. The patient had gained weight and shown great improvement in health over nine months. She had experienced mild twinges on three occasions. Dr. Dunlop drew attention to the rarity of the condition. He said that intussusception was a common sequel, and was more frequent with innocent growths than with malignant. The association with adenocarcinoma was unfortunately well established, as was that of the more common polyposis of the large intestine.

Carcinoma of the Colon.

Dr. Dunlop then presented a series of patients with carcinoma of the colon, illustrating methods of primary resection and anastomosis, assisted by the administration of phthalyl-sulphathiazole. In one case a secondary deposit was also resected from the liver. The patient was a male, aged sixty-three years, with a carcinoma of the transverse colon in which subacute obstruction had been precipitated by a barium meal. A single secondary deposit was noted in the overhanging right lobe of the liver. Primary resection of the growth, bowel anastomosis and "stab" caecostomy were carried out. As it was considered possible that the liver tumour was a direct implant it was subsequently resected. Nine months later the patient had gained two stone in weight and showed no evidence of recurrence.

The other patients were a male, aged sixty-five years, with a carcinoma of the recto-sigmoid junction, and a female, aged sixty-six years, with a carcinoma of the iliac colon. Wide resection and end-to-end anastomosis had been effected in each case.

A method of decompression was discussed whereby a rubber tube was passed through the rectum and guided into position just above the anastomosis. Dr. Dunlop stressed the fact that the departure from the established staged (defunctioning) procedures was still limited to selected subjects.

Modern Anæsthesia.

DR. BRIDGES WEBB AND DR. LENNARD TRAVERS demonstrated anæsthetic equipment and drew attention to the minimum requirements for the use of curare. The necessity for the anæsthetist to be in a position to control or at least to assist respiration during the administration of that drug was stressed. The various methods of anæsthesia were discussed and the equipment for their respective use was demonstrated.

Ophthalmological Demonstration.

DR. T. A'B. TRAVERS AND DR. NANCY LEWIS showed a series of patients of ophthalmological interest. There were a variety of types of retinitis, papillœdema and some congenital defects, some degenerative conditions and injuries. The patients were meant to illustrate the types of fundus conditions often seen in general practice.

Toxic Nodular Goitre.

DR. W. W. S. JOHNSTON showed two patients with toxic nodular goitre, treated with "thio" drugs and subsequently operated on.

The first patient was a woman, aged sixty-three years, who had been admitted to the Royal Melbourne Hospital on December 30, 1943, and had been one of an early series of subjects of toxic goitre treated with a "thio" drug (thiourea). She had been reported in the *Royal Melbourne Hospital Clinical Reports*, Volume XV, December, 1944, as having shown a satisfactory response. There had been a fall in basal metabolic rate from +45% to −12%, a fall in pulse rate and a rise in body weight, and the cardiac rhythm had reverted from auricular fibrillation to normal. In May, 1945, she had again been admitted to hospital, having discontinued thiourea for some months. There had been a return of toxic symptoms, with some degree of cardiac failure, and the basal metabolic rate had risen to +28%, the pulse rate being 112 per minute and the rhythm regular. She responded well to rest, digitalis and thiouracil, the latter being soon reduced to a maintenance dose of 0·2 gramme daily. For the next two years she attended as an out-patient, but her condition was found difficult to keep under control. By December, 1945, she had developed auricular fibrillation again and this had continued since. Even with small doses of thiouracil she showed a tendency to develop a condition of hypothyreoidism with a basal metabolic rate reduced to −18% and a slightly myxœdematous appearance. She appeared to benefit from small doses of thyreoid, but despite continuous digitalis therapy she developed congestive cardiac failure and was readmitted to the Royal Melbourne Hospital on June 18, 1947. At that time the pulse rate was 100 per minute, auricular fibrillation was present, she was fidgety and slightly tremulous, and the palms were moist. The basal metabolic rate was +30%. She then unexpectedly developed a condition of incipient thyreoid crisis, showing a confusional mental state, a temperature of 100·2° F. and a pulse rate of 120 per minute. She improved rapidly when treated with Lugol's solution and sedatives, her basal metabolic rate fell to −21%, and on July 14, 1947, she was submitted to subtotal thyreoidectomy, the response to the operation being immediately favourable. An interesting feature was that the gland, which on clinical examination showed little enlargement, was found at operation to be fleshy and much larger than had been supposed. Since then she had continued to feel much improved, though still showing auricular fibrillation. There was still a tendency to hypothyreoidism, and she was being treated with small doses of thyreoid gland.

Dr. Johnston's second patient was a woman, aged fifty-two years, who had been admitted to the Royal Melbourne Hospital on August 28, 1945, with a diagnosis of thyreotoxicosis and cardiac failure. For eighteen months she had had symptoms suggesting some degree of cardiac failure including shortness of breath and slight swelling of the

ankles. Over the twelve months before admission she had lost two stone in weight and during the last three months had become very irritable and easily upset. She had had chorea at the age of fourteen years. On examination she was found to have mitral stenosis and aortic regurgitation with enlargement of the heart and auricular fibrillation. No enlargement of the thyreoid gland was evident, but there was an obvious "stare" and a slight tremor of the outstretched fingers. In view of the fact that she had grave valvular defects due to old rheumatic infection as well as a myocardium affected by her existing thyreotoxicosis, it was decided that she would be a suitable subject for treatment by thiouracil, which was given for the last four weeks of her stay in hospital, the initial dose being 0·2 gramme thrice daily. On her discharge from hospital on October 10, 1945, the amount had been reduced to a maintenance dose of 0·2 gramme daily. During that period the basal metabolic rate had fallen from +27% to +5%. Concurrently she had been treated with "Neptal" and digitalis. She was discharged greatly improved, but auricular fibrillation persisted. Her improvement was maintained for some months, but she was readmitted to hospital on February 16, 1946. She had discontinued thiouracil two months previously, and, as her supply had finished, had not taken any digitalis for two weeks. On examination, the thyreoid gland was now found to be slightly enlarged and nodular, auricular fibrillation was present and the pulse rate was 120 per minute. There was some degree of congestive cardiac failure. The basal metabolic rate was +31%.

Dr. Johnston said that the problems presented by the patient at that stage had been, firstly, whether the auricular fibrillation and cardiac failure were dependent on the old rheumatic infection or on thyreotoxicosis, and, secondly, whether if thyreotoxicosis was responsible, the patient would be able to stand the strain of thyreoidectomy in view of the serious valvular lesions existing. After much consideration, thyreoidectomy had been decided on. Pre-operative treatment consisted of thiouracil 0·2 gramme daily for several weeks, followed by a course of Lugol's solution. On April 3, 1946, Dr. G. R. A. Syme performed subtotal thyreoidectomy. The patient came through the operation splendidly. Two days later auricular fibrillation was still present, though the heart rate was only between 70 and 80 per minute. Within one month auricular fibrillation had ceased, the rhythm was regular and the rate slow.

Calcium as a Therapeutic Agent.

Dr. Johnston's next patient was a girl, aged seventeen years, suffering from primary thyreotoxicosis. She had originally been admitted to the Royal Melbourne Hospital in December, 1946, with a history that initially she had been treated with thiouracil and had responded very well, the basal metabolic rate decreasing from +86% to +8%. But as the thyreoid gland had enlarged greatly after some weeks, thiouracil had been stopped and small doses of thyreoid given. With cessation of thiouracil the gland had decreased in size, but after two weeks toxic symptoms had recurred. Small doses of thiouracil had again resulted in diminution of toxic symptoms but increase in size of the thyreoid gland. Operation was therefore decided upon (the basal metabolic rate at that time being +40% and the thyreoid gland showing gross diffuse enlargement). Pre-operative medication by means of Lugol's solution was given for aproximately two weeks, and at the end of that time subtotal thyreoidectomy was carried out. The patient had been somewhat "toxic" up to the time of operation, her sleeping pulse rate being rarely below 100 per minute. Bleeding was troublesome at operation, the gland being diffusely enlarged and having, when cut, a pale pink and fleshy surface with much colloid. Blood transfusion was commenced about two hours after completion of operation, but a stormy post-operative period ensued marked by vomiting, tachycardia, a moderate grade of pyrexia and, later, jaundice. She improved with treatment by free fluids and intravenous administration of glucose-saline and Lugol's solution. Seven days after operation she suffered from an attack of tetany which was relieved promptly by an intravenous injection of calcium gluconate (ten millilitres of 10% solution). Calcium lactate was given by mouth, 60 grains twice daily, but a second attack of tetany occurred one week after the first. She was discharged from hospital on January 16, 1947. The serum calcium content was estimated just prior to that and found to be 9·5 milligrammes *per centum*.

Dr. Johnston said that over the next few months the patient had suffered from a number of sudden "turns", in some of which she fell down unconscious and bit her tongue. No history of any premonitory aura could be obtained, but the "turns" were preceded or accompanied by the *main d'accoucheur* sign. Diagnosis between tetany and epilepsy being difficult, the patient was readmitted to the Royal Melbourne Hospital on May 2, 1947, for observation and investigation. At that stage the serum calcium content was 6·0 milligrammes *per centum* and the serum phosphate content 4·1 milligrammes *per centum*. Those figures favoured tetany as the cause of the "turns", and that diagnosis was supported by such clinical tests as Trousseau's and Chvostek's. But, whatever the underlying condition might be, the indication clearly was to try to restore the normal blood chemistry in regard to calcium and phosphorus. To that end, three parathormone injections of 40, 30 and 30 units respectively were given at intervals of approximately eight hours, while calcium lactate by mouth and calcium gluconate by intramuscular injection were also given daily. Following the parathormone, dihydrotachysterol in the form of the Bayer preparation "A.T.10" was administered by mouth twice daily in doses varying from two to four millilitres. Dr. Johnston said that it was claimed that that drug, which was related chemically to ergosterol and to calciferol, had proved more uniformly effective than parathyreoid extract in the treatment of tetany, principally because of its more sustained action, so that after the blood calcium level had been restored to normal frequent administration was unnecessary. In the present instance it was decided to bring the blood calcium and phosphorus contents to normal levels as quickly as possible by means of parathormone and then, in order to avoid the tendency to the development of tolerance to that extract, to substitute treatment by "A.T.10". While the latter drug was being taken, the level of blood calcium rose from 6·7 to 7·2 milligrammes *per centum*, and that of the blood phosphorus fell from 5·0 to 3·5 milligrammes *per centum*. However, at that stage, in view of its comparatively small cost, calciferol was substituted with the satisfactory result that the blood calcium level rose to 9·2 milligrammes *per centum* and the blood phosphorus level fell to 3·2 milligrammes *per centum*. The calciferol was given by mouth in doses of 40,000 to 100,000 international units thrice daily. The patient's clinical condition showed gratifying improvement under that treatment. She had had one fit three days after admission to hospital, when the level of blood calcium was 6·3 milligrammes *per centum*; in that she had become unconscious and had bitten her tongue. Thereafter she had remained free of any such attacks; her outlook, which had been rather anxious and self-depreciatory, became distinctly brighter. During her stay in hospital various other investigations had been carried out. The fasting blood sugar level and the basal metabolic rate were found to be within normal limits, and an electroencephalogram when interpreted in the light of the history was thought to indicate that the attacks were epileptic in origin. The patient was discharged on June 18, 1947, with a blood calcium level of 9·2 milligrammes *per centum*, and she was instructed to continue taking calciferol by mouth in a dosage of 40,000 units thrice daily. Although the diagnosis was regarded as by no means clear between tetany and epilepsy, ultimately it was considered that a condition of tetany had arisen following thyreoidectomy and that that had been the precipitating factor in unmasking a latent state of epilepsy.

Dr. Johnston's last patient was a male, aged twenty-eight years, who had been admitted to the Royal Melbourne Hospital on June 26, 1947, with the provisional diagnosis of appendicitis. Further consideration of the clinical findings, together with the history of recent exposure to lead-containing fumes or dust, suggested the diagnosis of lead poisoning, which was confirmed by blood examination and a typical lead line in the gums of the lower jaw. Blood examination showed a hæmoglobin value of 72%, a total red blood cell count of 3,950,000 per cubic millimetre, and punctate basophilia to the degree of 32,000 per million red cells. There were no symptoms referable to the central nervous system. Immediate treatment consisted of an intravenous injection of fifteen millilitres of a 20% solution of calcium gluconate which quickly controlled the abdominal pain. The subsequent treatment was described at some length by Dr. Johnston during the ensuing discussion. He said that as was well known, it was usually based on the plan, firstly, of storing lead in the bones so that it would not be available to circulate freely and to give rise to the so-called "toxic episodes", and, secondly, a few weeks later, of eliminating some of the lead thus stored. Those objects were attained by firstly giving a diet of high calcium content, comprising such things as milk and eggs, with in addition doses of calcium lactate (75 grains daily), and then changing over to a diet of low calcium content with the addition of potassium iodide or ammonium chloride, the latter drug being effective by virtue of the acidosis induced. Stress was laid on the necessity for close observation of any

return of toxic manifestations which would necessitate a reversion to methods effecting storage of lead.

Dr. Johnston then referred to an alternative method of treatment for the details of which he was indebted to Dr. D. O. Shiels, of the Industrial Hygiene Division of the Victorian State Department of Health. That consisted of giving sodium citrate by mouth in doses of five grammes three times daily, without relation to any particular form of diet. It caused a fairly rapid elimination of lead, apparently without giving rise to toxic effects, and might be continued for several weeks during which a check was kept on the blood picture and other manifestations. The method had hardly as yet proved itself, but was attractive in its simplicity. Treatment in the present instance had been commenced in the conventional way with a diet of high calcium content and calcium lactate. After a few days sodium citrate treatment had been instituted and had been continued with satisfactory results. Some three weeks after the commencement of the administration of sodium citrate in full doses, the number of red blood cells had risen to 4,400,000 per cubic millimetre, and the number of stippled cells had fallen to 18,500 per million red cells. The hæmoglobin value had risen only slightly, from 67% to 72%. Toxic symptoms were in abeyance, though the lead line was still quite evident. The possible application of BAL (British Anti-Lewisite) to the treatment of lead poisoning was also referred to, though there was evidence, both experimental and therapeutic, that, in contradistinction to its value in arsenical poisoning, its use in plumbism might aggravate the toxic effects.

Post-Graduate Work.

THE POST-GRADUATE COMMITTEE IN MEDICINE IN THE UNIVERSITY OF SYDNEY.

SEMINAR IN MEDICAL STATISTICS.

THE Post-Graduate Committee in Medicine in the University of Sydney announces that Dr. H. O. Lancaster will hold a seminar in medical statistics on Wednesday, January 14, 1948, at 5.45 p.m., at the School of Public Health and Tropical Medicine, University grounds. The subject of the seminar will be "Biological Assays", and Miss Helen Newton Turner, of the Section of Mathematical Statistics, Council for Scientific and Industrial Research, will lead in the discussions.

These seminars are held on the second Wednesday of each month and any workers in medicine or related sciences are welcome to attend. If possible, data collected by members of the group will be discussed.

Naval, Military and Air Force.

APPOINTMENTS.

THE undermentioned appointments, changes *et cetera* have been promulgated in the *Commonwealth of Australia Gazette*, Number 241, of December 18, 1947.

AUSTRALIAN MILITARY FORCES.

Australian Army Medical Corps.

No. 115 (*Heidelberg*) *Military Hospital.*—The name of VX91437 Captain N. C. R. Merrillees is as now shown and not as it appeared in Executive Minute No. 131 of 1947, promulgated in *Commonwealth Gazette* No. 188 of 1947.

To be Temporary Major, 4th December, 1946.—NX200502 Captain D. H. Sutton.

No. 110 (*Perth*) *Military Hospital: To be Major, 7th June,* 1945.—VX39814 Captain S. E. Francis (in lieu of the notification respecting this officer which appeared in Executive Minute No. 114 of 1945, promulgated in *Commonwealth Gazette* No. 156A of 1945).

130*th Australian General Hospital: To be Temporary Major, 29th March,* 1947.—VX65418 Captain R. W. E. Hoyling.

Reserve Citizen Military Forces.

Australian Army Medical Corps.

1*st Military District.*—The following officers are retired, 4th August, 1947: Majors J. E. C. Aberdeen, J. R. Adam, W. V. Connor, C. F. Hecker, C. A. C. Leggett, M.B.E., C. R. Morton, G. W. Pottinger, H. A. Retallick, P. E. Voss, M.C., and D. Watson, Honorary Majors D. H. K. Lee, P. J. Monahan and D. E. Trumpy, Captains J. M. Allingham, J. A. L. Atkinson, P. Black, C. R. Boyce, G. H. Ellis, A. W. Frederick, A. S. Furness, J. L. Gorman, P. A. Hawken, T. G. Hewitt, W. A. L. T. Hyde, D. Macfie, M. E. Mackay, R. K. Macpherson, C. H. Mansfield, H. C. Murphy, T. R. Neville, C. L. Paine, C. T. Petherbridge, O. W. Powell, G. M. Redshaw, H. S. Roberts, L. S. Rudd, N. A. Sampson, J. C. Squires, J. Stewart, J. S. Sullivan, C. W. Taylor, A. R. Townsend, J. R. Turner, H. C. Wakefield and H. G. Wilson, Honorary Captains R. V. Adamson, L. W. Alderman, N. Aroney, H. D. Ashton, A. R. K. Burne, A. W. Chalmers, E. J. Gallagher, L. T. G. Geraghty, J. B. G. Gibson, N. F. George, W. S. Georgeson, V. E. Glover, L. Halberstater, J. J. Harris, A. Harrison, B. C. Harvey, F. Hatcher, J. W. P. Henderson, P. F. Hyndes, F. G. Lethbridge, W. F. Machin, A. M. Martell, W. J. Matthews, I. S. R. Munro, W. H. Nette, H. P. Palethorpe, R. Perkins, E. J. Ryan, H. B. Skinner, S. M. Stephenson, E. R. W. Thomson, J. J. Ward, C. G. Williams and N. V. Youngman.

ROYAL AUSTRALIAN AIR FORCE.

Citizen Air Force: Medical Branch.

William Deane-Butcher (261286) is appointed to a commission with the temporary rank of Squadron Leader, 17th October, 1947, for duty as an Ophthalmic Specialist, part time.

The appointment of Flight Lieutenant T. J. Thwaite (267766) is terminated on demobilization, 9th November, 1947.

Reserve: Medical Branch.

The appointment of Temporary Squadron Leader W. Deane-Butcher (261286) is terminated, 16th October, 1947.

Correspondence.

NEW TREATMENT OF RHEUMATOID ARTHRITIS.

SIR: I am rather interested in the article by Dr. Imre Barsi, of Buda-Pesth, in the *British Medical Journal*, August 16, 1947, on the treatment of rheumatoid arthritis by the transfusion of pregnant woman's blood. For years I have been convinced that both osteo and rheumatoid arthritis—more particularly the latter—are psychosomatic diseases with resultant endocrine disturbances (*British Medical Journal*, August 15, 1932, page 733).

Some time ago I asked Schering Proprietary, Limited, in Sydney to see if the Research Department of the Schering Corporation in the United States of America would undertake some investigations into the possible existence of an endocrine substance in the joints, and I have now asked them to try to isolate this potential hormone in pregnant blood.

I have written to Dr. Barsi, whom I think I once met at Saint Margaret's Island, for more detailed information. I hope the therapy is one-quarter as good as is implied. Meanwhile I should like to know if any of your readers have employed this treatment and with what results.

Yours, etc.,

231, Macquarie Street, Sydney,
December 15, 1947.

E. HASLETT FRAZER.

NURSES: THEIR RECRUITMENT AND TRAINING.

SIR: In a recent article on the shortage of nursing staff in the United Kingdom it was stated that the committee considering the question dealt first with the question whether there really was a shortage of nurses. The point of debate in this apparently self-evident question was whether the real problem was not the retaining of patients in bed or in hospital longer than necessary. We have been hearing for many years now of those who got their hernias up on the third or fourth day—their appendices on the first and midwifery cases in the first few days. I tended to regard these procedures previously with a certain amount of scepticism. But we now find an increasing volume of literature—not only

on the needlessness of bed rest but of its positive danger. In these circumstances it behoves the conservative majority of us to halt and consider whether this shortage of beds and nurses is not due more to our own obstinacy in refusing to use new methods than to a lack of volunteers for the noble profession or the failure of government planning.

It may be that there are some conditions that do still need complete bed rest as we know it, but one begins to doubt when one hears Professor Hugh Cairns saying of head injuries in *The Practitioner*:

> Early and graduated exercises, beginning within a few days of full recovery of consciousness, and proceeding by stages to full physical training gave better results than the older wholesale method of keeping the concussed patient in bed for three weeks.

And Professor Bramwell on heart conditions in the same journal:

> The cardiac patient must live right up to his limit of exercise tolerance, just as the athlete must do in order to attain the greatest physical efficiency of which he is capable.

I suggest that instead of complaining of shortage of beds and nurses we should start to study the effect of more early mobilization of bed cases, and I would respectfully suggest that you seek to publish in the journal more articles on the subject by those qualified to speak from their experience.

Yours, etc.,

N. F. BABBAGE.

Epping,
New South Wales,
December 19, 1947.

ZEITSCHRIFT FÜR VITAMINFORSCHUNG.

SIR: The *Zeitschrift für Vitaminforschung* of Berne is in future going to be an international journal of vitamin research. Dr. Gordonoff and Dr. Glanzmann are continuing as editors-in-chief, while Dr. Spies is the American editor, and I am the British editor. I should be most grateful if you would publish this letter, so that your readers may know that I should be glad to receive articles on vitamin research—either clinical, laboratory or veterinary. Further, short abstracts by the authors of articles on vitamin research published in Australia would be welcome for our section of abstracts.

Yours, etc.,

FRANKLIN BICKNELL.

14, Wimpole Street,
London, W.1,
November 27, 1947.

THE ROLE OF SPINAL FUSION IN ARTHROGENIC SCIATICA.

SIR: Mr. E. F. West (THE MEDICAL JOURNAL OF AUSTRALIA, December 13, 1947, page 711) has published his results without stating the occupations of his patients prior to their illness and without stating how many of them were compensatable. As this is of considerable significance I would be grateful if Mr. West would publish the relevant information.

Yours, etc.,

JAMES H. YOUNG.

131, Scarborough Beach Road,
Mt. Hawthorn,
Western Australia.
December 19, 1947.

A SOCIAL ASPECT OF THE Rh FACTOR.

SIR: A woman, aged twenty-two years, was seen by me at the ante-natal department of the Royal Hospital for Women, Paddington, eighteen weeks pregnant. She is unmarried, this is the first pregnancy, and there is no abnormality in the clinical obstetric findings. Her blood group is O4 Rh-negative.

She told me that it is her intention to carry on with the pregnancy and arrange for the adoption of the child. In view of the blood findings the warning was given that marriage with an Rh-positive husband might lead to future unsuccessful pregnancy. It was also impressed on her that during subsequent pregnancy the fact of this first one must not be concealed.

She is endeavouring to get in touch with the man responsible for the pregnancy to enable his Rh factor to be determined. Should this be negative her obstetric future is more secure.

The above story shows the necessity for determining the Rh factor in all primiparous women. This is now done as a routine in all women on their first visit to the ante-natal clinic at the Royal Hospital for Women.

Yours, etc.,

K. S. RICHARDSON.

Hengrove Hall,
193, Macquarie Street,
Sydney.
December 21, 1947.

POLIOMYELITIS IN PREVENTIVE ORTHOPÆDICS.

SIR: Dr. Jean Macnamara's article (December 13, 1947) on the possibility of the method of spread of poliomyelitis by means of milk will arouse widespread interest. In view of what she says, all householders would do well to scald their milk during the period of the epidemic. The question as to what should be done about ice-cream then arises. I would like to know if Dr. Macnamara has made quite certain that the milk used by the ice-cream manufacturers is not pasteurized. Ice-cream is made mainly by one or two manufacturers in each State, and it should be very easy to check up on this matter. The local agent of one of the big manufacturers assures me that the milk used by his firm is pasteurized not only once but twice. If this practice is carried out by all ice-cream manufacturers I would then like to know if Dr. Macnamara is satisfied, or if she still considers that there is a possibility of spread by this means.

Yours, etc.,

C. CRAIG,
Surgeon Superintendent.

General Hospital,
Launceston,
Tasmania.
December 22, 1947.

CONCERNING THE PATHOLOGY AND TREATMENT OF TENNIS ELBOW.

SIR: The article by Dr. J. R. S. Lahz in the current number of THE MEDICAL JOURNAL OF AUSTRALIA is a valuable contribution to the problem of tennis elbow. His remarks concerning the ætiology, anatomy and treatment of the condition are, in my opinion, substantially correct; his suggestion, however, that the essential pathology lies in the synovial membrane of the radio-humeral joint is, I consider, entirely wrong. Such a theory overlooks the fact that the same condition occasionally affects the medial epicondyle (where there is, of course, no joint) and that movement of the radio-humeral joint alone does not excite pain even when the condition is acute.

The condition as it occurs on the medial side is comparable in every way with lateral epicondylitis, except that the common flexor origin is involved instead of *extensor carpi radialis brevis* and *extensor digitorum*. In one personal case the pain was aggravated by flexing the middle finger against resistance, but not the other digits—indicating, I think, a very localized lesion in the flexor origin. The lesion must lie either in the tendons affected or in the periosteum at their insertion. I do not believe the hackneyed theory of partial tears in the tendon because frankly at operation they are never seen. Only once or twice have I seen synovial fringes as described by Dr. Lahz, and I note that he did not find them constantly. Usually no pathology is found.

I believe that the great majority of cases are traumatic and that in industry direct trauma is commoner than indirect strain in precipitating the condition. Commonly a man of strong muscular build sustains quite a slight blow on the elbow (the lateral epicondyle is more exposed and so more commonly injured than the medial epicondyle). At first the injury and pain seem trivial; in two days he may be unable to lift a cup of tea—the movements of grasping and of lifting with the forearm in pronation excite sharp pain. At the same time he may be able to lift a weight with the forearm supinated quite well.

If the essential lesion is a periostitis, it would be consistent with these physical signs. It would also explain the constant gnawing pain, the occasional periosteal reaction seen in X rays and the quick relief following any operation which divides the tendinous insertion. The difficulty is to explain the localized tenderness which varies, as Dr. Lahz states, and is not consistently over the epicondyle or the

radio-humeral joint, and the pain which radiates down the whole length of the forearm. Tension in the tendon excites it. What is it? A common condition respecting neither doctor nor patient lies one-quarter of an inch under the skin, still provokes us and still eludes us.

Yours, etc.,

HUGH C. BARRY.

British Medical Association House,
135, Macquarie Street,
Sydney.
December 22, 1947.

Obituary.

HERBERT HUFF JOHNSTON.

WE regret to announce the death of Dr. Herbert Huff Johnston, which occurred on December 26, 1947, at Sydney.

ALFRED JEFFERIS TURNER.

WE regret to announce the death of Dr. Alfred Jefferis Turner, which occurred on December 29, 1947, at Brisbane.

WILLIAM JOHN STEWART McKAY.

WE regret to announce the death of Dr. William John Stewart McKay, which occurred on January 3, 1948, at Lismore, New South Wales.

DAVID NEILSON KNOX.

WE regret to announce the death of Dr. David Neilson Knox, which occurred on January 3, 1948, at Hobart.

Nominations and Elections.

THE undermentioned have applied for election as members of the New South Wales Branch of the British Medical Association:

Carter, Mary, M.R.C.S. (England), L.R.C.P. (London), 1938, Ulundri, Old Castle Hill Road, Castle Hill.
Evans, Jack Lewis, provisional registration, 1947 (Univ. Sydney), Base Hospital, Dubbo.
Single, Denise Vallack, M.B., B.S., 1946 (Univ. Sydney), 19, Trelawney Street, Woollahra.
Golden, Albert Anthony, M.B., B.S., 1944 (Univ. Sydney), 13, Heydon Street, Mosman.
Deck, Philip Arnold, M.B., B.S., 1944 (Univ. Sydney), 3 Royal Australian Air Force Hospital, Concord.

Books Received.

"Cancer of the Breast", by Duncan C. L. Fitzwilliams, C.M.G., M.D., Ch.M., F.R.C.S. (Edinburgh and England); 1947. London: William Heinemann (Medical Books) Limited. 8¼" × 5½", pp. 208, with many illustrations. Price: 25s.

"Administration of Blood and Serum: Principles, Apparatus and Techniques"; 1947. Sydney: Red Cross Blood Transfusion Service, New South Wales. 8¼" × 5½", pp. 44, with illustrations. Distribution *gratis*.

Medical Appointments.

Dr. F. W. A. Clements has been appointed a member of the Council of the Canberra University College for a term ending on December 31, 1949.

The following medical officers have been appointed for a period of five years from December 1, 1947, to the St. Joseph's Hospital, Auburn, New South Wales: Consulting Surgeon, Dr. J. S. MacMahon; Physicians, Dr. E. M. McCaffrey, Dr. C. E. Fitzgerald, Dr. R. I. Eakin and Dr. B. Curtin; Surgeons, Dr. R. Sheldon, Dr. C. A. McDermott, Dr. K. J. Fagan and Dr. C. F. Bellemore; Orthopædic Surgeon, Dr. R. J. B. McEwen; Ear, Nose and Throat Surgeon, Dr. H. J. Eizenberg; Urologist, Dr. E. G. Maloney; Pathologist, Dr. J. Garvan; Radiologist, Dr. C. Cole; Anæsthetists, Dr. J. Levy and Dr. B. Mooney.

Dr. E. C. M. Wallace has been appointed assistant medical officer of health, Department of Public Health, New South Wales.

Diary for the Month.

JAN. 15.—Victorian Branch, B.M.A.: Organization Subcommittee.
JAN. 19.—Victorian Branch, B.M.A.: Finance, House and Library Subcommittee Meeting.
JAN. 22.—Victorian Branch, B.M.A.: Executive Meeting.
JAN. 23.—Queensland Branch, B.M.A.: Council Meeting.
JAN. 28.—Victorian Branch, B.M.A.: Council Meeting.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Honorary Secretary, 135, Macquarie Street, Sydney): Australian Natives' Association; Ashfield and District United Friendly Societies' Dispensary; Balmain United Friendly Societies' Dispensary; Leichhardt and Petersham United Friendly Societies' Dispensary; Manchester Unity Medical and Dispensing Institute, Oxford Street, Sydney; North Sydney Friendly Societies' Dispensary Limited; People's Prudential Assurance Company Limited; Phœnix Mutual Provident Society.

Victorian Branch (Honorary Secretary, Medical Society Hall, East Melbourne): Associated Medical Services Limited; all Institutes or Medical Dispensaries; Australian Prudential Association, Proprietary, Limited; Federated Mutual Medical Benefit Society; Mutual National Provident Club; National Provident Association; Hospital or other appointments outside Victoria.

Queensland Branch (Honorary Secretary, B.M.A. House, 225, Wickham Terrace, Brisbane, B.17): Brisbane Associated Friendly Societies' Medical Institute; Bundaberg Medical Institute; Brisbane City Council (Medical Officer of Health). Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

South Australian Branch (Honorary Secretary, 178, North Terrace, Adelaide): All Lodge appointments in South Australia; all Contract Practice appointments in South Australia.

Western Australian Branch (Honorary Secretary, 205, Saint George's Terrace, Perth): Wiluna Hospital; all Contract Practice appointments in Western Australia. All government appointments with the exception of those of the Department of Public Health.

Editorial Notices.

MANUSCRIPTS forwarded to the office of this journal cannot under any circumstances be returned. Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary be stated.

All communications should be addressed to the Editor, THE MEDICAL JOURNAL OF AUSTRALIA, The Printing House, Seamer Street, Glebe, New South Wales. (Telephones: MW 2651-2.)

Members and subscribers are requested to notify the Manager, THE MEDICAL JOURNAL OF AUSTRALIA, Seamer Street, Glebe, New South Wales, without delay, of any irregularity in the delivery of this journal. The management cannot accept any responsibility or recognize any claim arising out of non-receipt of journals unless such notification is received within one month.

SUBSCRIPTION RATES.—Medical students and others not receiving THE MEDICAL JOURNAL OF AUSTRALIA in virtue of membership of the Branches of the British Medical Association in the Commonwealth can become subscribers to the journal by applying to the Manager or through the usual agents and booksellers. Subscriptions can commence at the beginning of any quarter and are renewable on December 31. The rates are £2 for Australia and £2 5s. abroad per annum payable in advance.